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SESSION RESUMED IN FILE 'HOME' AT 17:01:57 ON 11 AUG 2009

FILE 'HOME' ENTERED AT 17:01:57 ON 11 AUG 2009

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.66	0.66

=> FILE REG

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.88	0.88

FILE 'REGISTRY' ENTERED AT 17:02:23 ON 11 AUG 2009

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STRUCTURE FILE UPDATES: 10 AUG 2009 HIGHEST RN 1173881-48-5

DICTIONARY FILE UPDATES: 10 AUG 2009 HIGHEST RN 1173881-48-5

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<http://www.cas.org/support/stngen/stndoc/properties.html>

=> S rofecoxib/CN

L1 1 ROFECOXIB/CN

=> D L1

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN

RN 162011-90-7 REGISTRY

ED Entered STN: 07 Apr 1995

CN 2(5H)-Furanone, 4-[4-(methanesulfonyl)phenyl]-3-phenyl- (CA INDEX NAME)

OTHER NAMES:

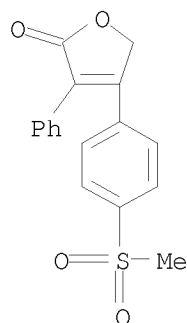
CN 3-(4-Methanesulfonylphenyl)-2-phenyl-2-buten-4-olide

CN 3-Phenyl-4-[4-(Methanesulfonyl)phenyl]-2(5H)-furanone

CN 4-(4-(Methanesulfonyl)phenyl)-3-phenyl-5H-furan-2-one

CN 4-[(4-Methanesulfonyl)phenyl]-3-phenyl-2(5H)-furanone

CN MK 0966
 CN MK 966
 CN Rhuma-cure
 CN Rofecoxib
 CN Vioxx
 DR 186912-82-3
 MF C17 H14 O4 S
 CI COM
 SR CA
 LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO,
 CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, EMBASE,
 HSDB*, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE,
 MRCK*, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER,
 USAN, USPAT2, USPATFULL
 (*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2203 REFERENCES IN FILE CA (1907 TO DATE)
 56 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 2208 REFERENCES IN FILE CAPLUS (1907 TO DATE)

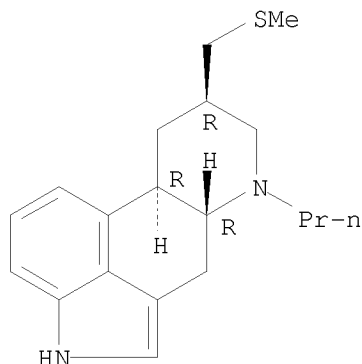
=> S pergolide/CN
 L2 1 PERGOLIDE/CN

=> D L2

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
 RN 66104-22-1 REGISTRY
 ED Entered STN: 16 Nov 1984
 CN Ergoline, 8-[(methylthio)methyl]-6-propyl-, (8 β)- (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN Indolo[4,3-fg]quinoline, ergoline deriv.
 OTHER NAMES:
 CN D-8 β -[(Methylthio)methyl]-6-propylergoline
 CN LY 141B
 CN Pergolide
 FS STEREOSEARCH
 MF C19 H26 N2 S
 CI COM
 LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS,
 BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM,
 DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH,
 IPA, MEDLINE, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*,

SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

709 REFERENCES IN FILE CA (1907 TO DATE)
11 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
710 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> S selegiline/CN

L3 1 SELEGILINE/CN

=> D L3

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN

RN 14611-51-9 REGISTRY

ED Entered STN: 16 Nov 1984

CN Benzeneethanamine, N, α -dimethyl-N-2-propyn-1-yl-, (α R)- (CA
INDEX NAME)

OTHER CA INDEX NAMES:

CN Benzeneethanamine, N, α -dimethyl-N-2-propynyl-, (α R)- (9CI)

CN Benzeneethanamine, N, α -dimethyl-N-2-propynyl-, (R)-

CN Phenethylamine, N, α -dimethyl-N-2-propynyl-, L-(-)- (8CI)

OTHER NAMES:

CN (-)-Deprenil

CN (-)-Deprenyl

CN (-)-Selegiline

CN (R)-(-)-Deprenyl

CN (R)-Selegiline

CN Anipryl

CN Emsam TTS

CN l-Deprenyl

CN L-Deprenyl

CN Selegiline

CN Selgene

CN Zelapar

FS STEREOSEARCH

DR 172964-89-5

MF C13 H17 N

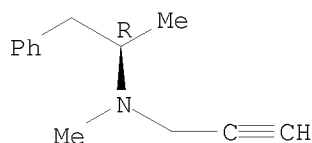
CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSDRUGNEWS, IMSPATENTS, IMSPRODUCT, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, USPATOLD, VETU

(*File contains numerically searchable property data)

Other Sources: WHO

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1428 REFERENCES IN FILE CA (1907 TO DATE)

26 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1432 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> FILE MEDICINE

FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

22.68

23.56

FILE 'ADISCTI' ENTERED AT 17:03:15 ON 11 AUG 2009

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PROCESSING COMPLETED FOR L5
L6 3 DUP REM L5 (7 DUPLICATES REMOVED)

=> D 1-3 IBIB ABS

L6 ANSWER 1 OF 3 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
DUPLICATE 1

ACCESSION NUMBER: 2004:56984 BIOSIS

DOCUMENT NUMBER: PREV200400059117

TITLE: Additive neuroprotective effects of creatine and a
cyclooxygenase 2 inhibitor against dopamine depletion in
the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)
mouse model of Parkinson's disease.

AUTHOR(S): Klivenyi, Peter; Gardian, Gabrielle; Calingasan, Noel Y.;
Yang, Lichuan; Beal, M. Flint [Reprint Author]

CORPORATE SOURCE: Department of Neurology and Neuroscience, Weill Medical
College of Cornell University, New York-Presbyterian
Hospital, New York, NY, 10021, USA
fbeal@med.cornell.edu

SOURCE: Journal of Molecular Neuroscience, (2003) Vol.
21, No. 3, pp. 191-198. print.
E-ISSN: 0895-8696 (ISSN online).

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 21 Jan 2004

Last Updated on STN: 21 Jan 2004

AB There is evidence that both inflammatory mechanisms and mitochondrial
dysfunction contribute to Parkinson's disease (PD) pathogenesis.
We investigated whether the cyclooxygenase 2 (COX-2) inhibitor
rofecoxib either alone or in combination with creatine could exert
neuroprotective effects in the 1-methyl-4-phenyl-1,2,3,
6-tetrahydropyridine model of PD in mice. Both rofecoxib and
creatine administered alone protected against striatal dopamine depletions
and loss of substantia nigra tyrosine hydroxylase immunoreactive neurons.
Administration of rofecoxib with creatine produced significant
additive neuroprotective effects against dopamine depletions. These
results suggest that a combination of a COX-2 inhibitor with creatine
might be a useful neuroprotective strategy for PD.

L6 ANSWER 2 OF 3 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:203937 BIOSIS

DOCUMENT NUMBER: PREV200400204480

TITLE: Selective COX - 2 inhibitors reduce MPTP - induced
neurotoxicity.

AUTHOR(S): Vijitruth, R. [Reprint Author]; Liu, M. [Reprint Author];
Choi, D. Y. [Reprint Author]; Kulik, C. M. [Reprint
Author]; Bing, G. Y. [Reprint Author]

CORPORATE SOURCE: Dept. of Anat. and NeuroBiol., Univ. of Kentucky,
Lexington, KY, USA

SOURCE: Society for Neuroscience Abstract Viewer and Itinerary
Planner, (2003) Vol. 2003, pp. Abstract No.
732.5. <http://sfn.scholarone.com>. e-file.
Meeting Info.: 33rd Annual Meeting of the Society of
Neuroscience. New Orleans, LA, USA. November 08-12, 2003.
Society of Neuroscience.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 14 Apr 2004

Last Updated on STN: 14 Apr 2004

AB Parkinson's Disease (PD) is caused by the degradation of
dopaminergic neurons in the substantia nigra pars compacta (SNpc), and

inflammation has been proposed to play an important role in the progression of the disease. Cyclooxygenase (COX) is an enzyme that catalyzes production of prostanoid products from arachidonic acid, and the inducible isoform, COX-2, is believed to play a key role in the inflammatory response. To determine if inhibitors of COX-2 activity can improve survival of dopaminergic neurons in the SNpc and reduce activation of microglial cells after 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) injection, C57BL/6 mice were treated with one of three COX-2 selective inhibitors (COXIBs): Celebrex (celecoxib), Vioxx (rofecoxib), or Bextra (valdecoxib). COXIBs (30 mg/kg daily in food supplement) were administered for the duration of the study, starting 2 weeks before saline or MPTP injection (15 mg/kg 4 times at 1.5 hr intervals, i.p.). MPTP can replicate most of the characteristic features of PD including nigral dopaminergic cell death and microglial activation. In the current study, COX-2 inhibitors protected SNpc dopaminergic neurons from MPTP neurotoxicity, as revealed by tyrosine hydroxylase (TH) immunoreactivity. In addition, all three COXIBs proved effective in reducing microglial activation. Inhibition of COX-2 also improved measures of locomotor activity recorded by automated activity monitors. The data indicate that reducing activity of COX-2 can mitigate dopaminergic cell death caused by MPTP, possibly by suppression of microglia-dependent inflammatory pathways, suggesting COX-2 inhibitors as potential therapeutic drugs for interventional treatment of PD.

L6 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
 ACCESSION NUMBER: 2003:325652 BIOSIS
 DOCUMENT NUMBER: PREV200300325652
 TITLE: PHARMACOLOGICAL INHIBITION OF COX - 2 PROVIDES

NEUROPROTECTION IN THE MPTP - MOUSE MODEL OF PARKINSON'S DISEASE.

AUTHOR(S): Teismann, P. [Reprint Author]; Jackson-Lewis, V. [Reprint Author]; Tieu, K. [Reprint Author]; Vila, M. [Reprint Author]; Przedborski, S. [Reprint Author]

CORPORATE SOURCE: Neurology, Pathology, Columbia Univ, College of Physicians and Surgeons, New York, NY, USA

SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 690.17. <http://sfn.scholarone.com.cd-rom>. Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002. Society for Neuroscience.

DOCUMENT TYPE: Conference; (Meeting)
 Conference; (Meeting Poster)
 Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 16 Jul 2003

Last Updated on STN: 16 Jul 2003

AB Neuroinflammation is believed to play a deleterious role in Parkinson's disease (PD) and in its experimental model produced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). In keeping with this, we have shown that mice deficient in cyclooxygenase-2 (COX-2), one of the enzymes producing the pro-inflammatory prostaglandin PGE2, are more resistant to MPTP. Now we demonstrate that inhibition of COX-2 by rofecoxib also provides significant neuroprotection in MPTP-treated mice. Five days before and after an acute regimen of MPTP (4x20 mg/kg i.p., 2 h apart), C57BL/6 mice received 25 mg/kg rofecoxib orally, which is a regimen that reduces MPTP-related ventral midbrain PGE2 levels by 23%. Seven days after MPTP treatment, the status of the nigrostriatal pathway was assessed by immunohistochemistry for tyrosine hydroxylase (TH). MPTP-treated mice, which received rofecoxib showed significantly more TH-positive neurons in the substantia nigra than those which did not (saline: 9,656 ± 322;

rofecoxib: 9,020 442; MPTP/saline: 3,933 798; MPTP/rofecoxib: 6673 601; values are mean S.E.M.). Although less striking, rofecoxib provided significant protection against MPTP-induced striatal TH-positive terminal loss. Associated with the attenuation of MPTP-induced nigrostriatal degeneration, rofecoxib abated markers of neuroinflammation. These data are consistent with the notion that neuroinflammation participates in neurodegeneration and suggest that blockade of COX-2 may be a valuable strategy for neuroprotective therapies for PD.

=> S pergolide/ab and (PARKINSON? OR ANTIPARKINSON?)/AB

[illegible]

L7 2091 PERGOLIDE/AB AND (PARKINSON? OR ANTIPARKINSON?)/AB

=> S L7 and pd<2003

6 FILES SEARCHED...

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'2003' NOT A VALID FIELD CODE
'2003' NOT A VALID FIELD CODE
'2003' NOT A VALID FIELD CODE
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18 FILES SEARCHED...

'2003' NOT A VALID FIELD CODE

22 FILES SEARCHED...

'2003' NOT A VALID FIELD CODE

'2003' NOT A VALID FIELD CODE

30 FILES SEARCHED...

L8 1122 L7 AND PD<2003

=> DUP REM L8

DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DGENE, DRUGMONOG2, IMSPRODUCT, KOSMET, NUTRACEUT, PCTGEN, PHARMAML, USGENE'.

ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIOQUE

PROCESSING IS APPROXIMATELY 79% COMPLETE FOR L8

PROCESSING COMPLETED FOR L8

L9 331 DUP REM L8 (791 DUPLICATES REMOVED)

$\Rightarrow S \text{ L9 and L1}$

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'CN' IS NOT A VALID FIELD CODE
'CN' IS NOT A VALID FIELD CODE
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'CN' IS NOT A VALID FIELD CODE
'CN' IS NOT A VALID FIELD CODE
'CN' IS NOT A VALID FIELD CODE
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[illegible]

=> D L9 1-20 IBIB ABS

ACCESSION NUMBER: 2002:415157 BIOSIS
DOCUMENT NUMBER: PREV200200415157
TITLE: Sleep attacks in patients taking dopamine agonists: Review.
AUTHOR(S): Homann, Carl Nikolaus [Reprint author]; Wenzel, Karoline;
Suppan, Klaudia; Ivanic, Gerd; Kriechbaum, Norbert;
Crevenna, Richard; Ott, Erwin
CORPORATE SOURCE: Department of Neurology, Karl Franzens University Hospital,
A-8036, Graz, Austria
nik.homann@kfunigraz.ac.at
SOURCE: BMJ, (22 June, 2002) Vol. 324, No. 7352, pp.
1483-1487. print.
ISSN: 0959-8138.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jul 2002
Last Updated on STN: 23 Sep 2002

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CORPORATE SOURCE: Homann, Carl Nikolaus; Wenzel, Karoline; Suppan, Klaudia; Ivanic, Gerd; Crevenna, Richard; Ott, Erwin; Kriechbaum, Norbert (Department of Neurology, Karl Franzens University Hospital, A-8036 Graz (AT))

SOURCE: British Medical Journal (22 Jun 2002) Volume 324, Number 7352, pp. 1483-1487, 34 refs.
CODEN: BMJOAE ISSN: 0959-8146

COUNTRY OF PUBLICATION: United Kingdom

DOCUMENT TYPE: Journal; Article

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 1 Feb 2009
Last updated on STN: 1 Feb 2009

AN 2002143570 ESBIODBASE

AB Objectives: To assess the evidence for the existence and prevalence of sleep attacks in patients taking dopamine agonists for Parkinson's disease, the type of drugs implicated, and strategies for prevention and treatment. Design: Review of publications between July 1999 and May 2001 in which sleep attacks or narcoleptic-like attacks were discussed in patients with Parkinson's disease. Results: 124 patients with sleep events were found in 20 publications. Overall, 6.6% of patients taking dopamine agonists who attended movement disorder centres had sleep events. Men were over-represented. Sleep events occurred at both high and low doses of the drugs, with different durations of treatment (0-20 years), and with or without preceding signs of tiredness. Sleep attacks are a class effect, having been found in patients taking the following dopamine agonists: levodopa (monotherapy in 8 patients), ergot agonists (apomorphine in 2 patients, bromocriptine in 13, cabergoline in 1, lisuride or pramipexole in 23, pergolide in 5,) and non-ergot agonists (pramipexole in 32, ropinirole in 38). Reports suggest two distinct types of events: those of sudden onset without warning and those of slow onset with prodrome drowsiness. Conclusion: Insufficient data are available to provide effective guidelines for prevention and treatment of sleep events in patients taking dopamine agonists for Parkinson's disease. Prospective population based studies are needed to provide this information.

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ACCESSION NUMBER: 2003:45771 BIOSIS

DOCUMENT NUMBER: PREV200300045771

TITLE: An evidence-based review of dopamine receptor agonists in the treatment of Parkinson's disease.

AUTHOR(S): Deleu, Dirk [Reprint Author]; Northway, Margaret G.; Hanssens, Yolande

CORPORATE SOURCE: College of Medicine, Sultan Qaboos University, PO Box 35, Al Khod, PC-123, Sultanate of Oman
dtodeleu@squ.edu.om

SOURCE: Saudi Medical Journal, (October 2002) Vol. 23, No. 10, pp. 1165-1175. print.
ISSN: 0379-5284.

DOCUMENT TYPE: Article
General Review; (Literature Review)

LANGUAGE: English

ENTRY DATE: Entered STN: 15 Jan 2003
Last Updated on STN: 15 Jan 2003

AB Apomorphine and certain ergot alkaloids (bromocriptine, lisuride and pergolide) have been available for several decades; for the last few years, they were joined by newer dopamine agonists (cabergoline, pramipexole and ropinirole) most of them are non-ergolines. Each of these dopamine agonists has its own pharmacological characteristics and occupies a place in the pharmacotherapy of Parkinson's disease. In this

evidence-based review, emphasis is put on the clinical efficacy of dopamine agonists in early and advanced Parkinson's disease, and where possible comparative evidence regarding their efficacy and safety is provided. In addition, their clinical pharmacokinetics, adverse effect profiles and most relevant interactions will be summarized.

L9 ANSWER 4 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 3

ACCESSION NUMBER: 2003143110 EMBASE
TITLE: [Multiple latency test in a patient with episodes of sleep induced by pergolide].
Test de latencias multiples en un paciente con episodios de sueno inducidos por pergolida.
AUTHOR: Jimenez-Jimenez, Felix Javier, Dr. (correspondence); De Toledo, M.; Sayed, Y.; Zurdo, M.
CORPORATE SOURCE: Servicio de Neurologia, Hospital Principe de Asturias, Universidad de Alcala, Alcala de Henares, Madrid, Spain. fjimenezj@meditex.es
AUTHOR: Jimenez-Jimenez, Felix Javier, Dr. (correspondence); Velasco, I.; Orti-Pareja, M.
CORPORATE SOURCE: Neuro-Magister SL Co., Madrid, Spain. fjimenezj@meditex.es
AUTHOR: Jimenez-Jimenez, Felix Javier, Dr. (correspondence)
CORPORATE SOURCE: Corregidor Jose de Pasamonte 24 3 D., E-28030 Madrid, Spain . fjimenezj@meditex.es
AUTHOR: Jimenez-Jimenez, Felix Javier, Dr. (correspondence)
CORPORATE SOURCE: Corregidor Jose de Pasamonte 24 3 D., E-28030 Madrid, Spain . fjimenezj@meditex.es
SOURCE: Revista de Neurologia, (16 Jun 2002) Vol. 34, No. 12, pp. 1140-1141.
Refs: 10
ISSN: 0210-0010 CODEN: RVNRAA
COUNTRY: Spain
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: Spanish; Castilian
SUMMARY LANGUAGE: English; Spanish; Castilian; Portuguese
ENTRY DATE: Entered STN: 17 Apr 2003
Last Updated on STN: 17 Apr 2003

AB Objective. Recently, there have been report 'sleep attacks' in parkinsonian patients as a side-effect of pramipexole and ropinirole. We report a patient with similar episodes related with pergolide. Case report. A 64 year-old man with rigidakinetic parkinsonism, treated with carbidopa/levodopa and pergolide, developed sudden, irresistible sleep episodes after increasing the dose of pergolide to 2.25 mg/day because of bad control of parkinsonian symptoms. These episodes started 30 minutes after each dose of pergolide and lasted 2 hours. Following reduction of the dose of pergolide to 1.5 mg/day the sleep episodes disappeared. Two double-blind multiple sleep latency tests were performed, one after intalaking pergolide and other after intaking placebo. Results. The latencies to sleep onset were lower with pergolide than with placebo, but the differences did not reach statistical significance. There was no premature REM sleep onset. Conclusion. Sleep episodes are likely a not specific effect of dopamine agonists.

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ACCESSION NUMBER: 2003:172061 BIOSIS
DOCUMENT NUMBER: PREV200300172061

TITLE: Differential actions of antiparkinson agents at multiple classes of monoaminergic receptor. III. Agonist and antagonist properties at serotonin, 5-HT1 and 5-HT2, receptor subtypes.

AUTHOR(S): Newman-Tancredi, Adrian; Cussac, Didier; Quentric, Yann; Touzard, Manuelle; Verrielle, Laurence; Carpentier, Nathalie; Millan, Mark J. [Reprint Author]

CORPORATE SOURCE: Institut de Recherches Servier, Centre de Recherches de Croissy, 125 chemin de Ronde, Croissy/Seine, 78290, Paris, France
mark.millan@fr.netgrs.com

SOURCE: Journal of Pharmacology and Experimental Therapeutics, (November 2002) Vol. 303, No. 2, pp. 815-822. print.
ISSN: 0022-3565 (ISSN print).

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 2 Apr 2003
Last Updated on STN: 2 Apr 2003

AB Although certain antiparkinson agents interact with serotonin (5-HT) receptors, little information is available concerning functional actions. Herein, we characterized efficacies of apomorphine, bromocriptine, cabergoline, lisuride, piribedil, pergolide, roxindole, and terguride at human (h)5-HT1A, h5-HT1B, and h5-HT1D, receptors (guanosine 5'-O-(3-(35S)thio)triphosphate ((35S)GTPgammaS) binding), and at h5-HT2A, h5-HT2B, and h5-HT2C receptors (depletion of membrane-bound (3H)phosphatidylinositol). All drugs stimulated h5-HT1A receptors with efficacies (compared with 5-HT, 100%) ranging from modest (apomorphine, 35%) to high (cabergoline, 93%). At h5-HT1B receptors, efficacies varied from mild (terguride, 37%) to marked (cabergoline, 102%) and potencies were modest (pEC50 values of 5.8-7.6): h5-HT1D sites were activated with a similar range of efficacies and greater potency (7.1-8.5). Piribedil and apomorphine were inactive at h5-HT1B and h5-HT1D receptors. At h5-HT2A receptors, terguride, lisuride, bromocriptine, cabergoline, and pergolide displayed potent (7.6-8.8) agonist properties (49-103%), whereas apomorphine and roxindole were antagonists and piribedil was inactive. Only pergolide (113%/8.2) and cabergoline (123%/8.6) displayed pronounced agonist properties at h5-HT2B receptors. At 5-HT2C receptors, lisuride, bromocriptine, pergolide, and cabergoline were efficacious (75-96%) agonists, apomorphine and terguride were antagonists, and piribedil was inactive. MDL100,907 and SB242,084, selective antagonists at 5-HT2A and 5-HT2C receptors, respectively, abolished these actions of pergolide, cabergoline, and bromocriptine. In conclusion, antiparkinson agents display markedly different patterns of agonist and antagonist properties at multiple 5-HT receptor subtypes. Although all show modest (agonist) activity at 5-HT1A sites, their contrasting actions at 5-HT2A and 5-HT2C sites may be of particular significance to their functional profiles in vivo.

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STN DUPLICATE 5

ACCESSION NUMBER: 2003:172060 BIOSIS

DOCUMENT NUMBER: PREV200300172060

TITLE: Differential actions of antiparkinson agents at multiple classes of monoaminergic receptor. II. Agonist and antagonist properties at subtypes of dopamine D2-like receptor and alpha1/alpha2-adrenoceptor.

AUTHOR(S): Newman-Tancredi, Adrian; Cussac, Didier; Audinot, Valerie; Nicolas, Jean-Paul; De Ceuninck, Frederic; Boutin, Jean-A.; Millan, Mark J. [Reprint Author]

CORPORATE SOURCE: Institut de Recherches Servier, Centre de Recherches de Croissy, 125 chemin de Ronde, Croissy/Seine, Paris, 78290,

France
mark.millan@fr.netgrs.com

SOURCE: Journal of Pharmacology and Experimental Therapeutics, (November 2002) Vol. 303, No. 2, pp. 805-814. print.
ISSN: 0022-3565 (ISSN print).

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 2 Apr 2003
Last Updated on STN: 2 Apr 2003

AB The accompanying multivariate analysis of the binding profiles of antiparkinson agents revealed contrasting patterns of affinities at diverse classes of monoaminergic receptor. Herein, we characterized efficacies at human (h)D2SHORT(S), hD2LONG(L), hD3, and hD4.4 receptors and at halpha2A-, halpha2B-, halpha2C-, and halpha1A-adrenoceptors (ARs). As determined by guanosine 5'-O-(3-(35S)thio)triphosphate ((35S)GTPgammaS) binding, no ligand displayed "full" efficacy relative to dopamine (100%) at all "D2-like" sites. However, at hD2S receptors quinpirole, pramipexole, ropinirole, quinerolane, pergolide, and cabergoline were as efficacious as dopamine (Emaxgtoreq 100%); TL99, talipexole, and apomorphine were highly efficacious (79-92%); piribedil, lisuride, bromocriptine, and terguride showed intermediate efficacy (40-55%); and roxindole displayed low efficacy (11 %). For all drugs, efficacies were lower at hD2L receptors, with terguride and roxindole acting as antagonists. At hD3 receptors, efficacies ranged from 33% (roxindole) to 94% (TL99), whereas, for hD4 receptors, highest efficacies (apprx70%) were seen for quinerolane, quinpirole, and TL99, whereas piribedil and terguride behaved as antagonists and bromocriptine was inactive. Although efficacies at hD2S versus hD2L sites were highly correlated (r = 0.79), they correlated only modestly to hD3/hD4 sites (r = 0.44-0.59). In (35S)GTPgammaS studies of halpha2A-ARs, TL99 (108%), pramipexole (52%), talipexole (51%), pergolide (31%), apomorphine (16%), and quinerolane (11%) were agonists and ropinirole and roxindole were inactive, whereas piribedil and other agents were antagonists. Similar findings were obtained at halpha2B- and halpha2C-ARs. Using (3H)phosphatidylinositol depletion, roxindole, bromocriptine, lisuride, and terguride displayed potent antagonist properties at halpha1A-ARs. In conclusion, antiparkinson agents display diverse agonist and antagonist properties at multiple subtypes of D2-like receptor and alpha1/alpha2-AR, actions, which likely contribute to their contrasting functional profiles.

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STN DUPLICATE 6

ACCESSION NUMBER: 2003:172059 BIOSIS

DOCUMENT NUMBER: PREV200300172059

TITLE: Differential actions of antiparkinson agents at multiple classes of monoaminergic receptor. I. A multivariate analysis of the binding profiles of 14 drugs at 21 native and cloned human receptor subtypes.

AUTHOR(S): Millan, Mark J. [Reprint Author]; Maiofiss, Lisa; Cussac, Didier; Audinot, Valerie; Boutin, Jean-A.; Newman-Tancredi, Adrian

CORPORATE SOURCE: Institut de Recherches Servier, Centre de Recherches de Croissy, 125 chemin de Ronde, Croissy/Seine, 78290, Paris, France
mark.millan@fr.netgrs.com

SOURCE: Journal of Pharmacology and Experimental Therapeutics, (November 2002) Vol. 303, No. 2, pp. 791-804. print.
ISSN: 0022-3565 (ISSN print).

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 2 Apr 2003

Last Updated on STN: 2 Apr 2003

AB Because little comparative information is available concerning receptor profiles of antiparkinson drugs, affinities of 14 agents were determined at diverse receptors implicated in the etiology and/or treatment of Parkinson's disease: human (h)D1, hD2S, hD2L, hD3, hD4, and hD5 receptors; human 5-hydroxytryptamine (5-HT)1A, h5-HT1B, h5-HT1D, h5-HT2A, h5-HT2B, and h5-HT2C receptors; halphalA-, halphalB-, halphalD-, halpha2A-, halpha2B-, halpha2C-, rat alpha2D-, hbeta1-, and hbeta2-adrenoceptors (ARs); and native histamine1, receptors. A correlation matrix (294 pKi values) demonstrated substantial "co-variance". Correspondingly, principal components analysis revealed that axis 1, which accounted for 76% variance, was associated with the majority of receptor types: drugs displaying overall high versus modest affinities migrated at opposite extremities. Axis 2 (7% of variance) differentiated drugs with high affinity for hD4 and H1 receptors versus halphal-AR subtypes. Five percent of variance was attributable to axis 3, which distinguished drugs with marked affinity for hbeta1- and hbeta2-ARs versus hD5 and 5-HT2A receptors. Hierarchical (cluster) analysis of global homology generated a dendrogram differentiating two major groups possessing low versus high affinity, respectively, for multiple serotonergic and hD5 receptors. Within the first group, quinpirole, quinerolane, ropinirole, and pramipexole interacted principally with hD2, hD3, and hD4 receptors, whereas piribedil and talipexole recognized dopaminergic receptors and halpha2-ARs. Within the second group, lisuride and terguride manifested high affinities for all sites, with roxindole/bromocriptine, cabergoline/pergolide, and 6,7-dihydroxy-N,N-dimethyl-2-ammotetralin (TL99)/apomorphine comprising three additional subclusters of closely related ligands. In conclusion, an innovative multivariate analysis revealed marked heterogeneity in binding profiles of antiparkinson agents. Actions at sites other than hD2 receptors likely participate in their (contrasting) functional profiles.

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ACCESSION NUMBER: 2003131039 EMBASE
TITLE: Pergolide-induced pleural effusion in a patient with juvenile parkinsonism.
AUTHOR: Kuwabara, Takeo, Dr. (correspondence)
CORPORATE SOURCE: Department of Neurology, Niigata Prefectural Shibata Hospital, Niigata, Japan.
SOURCE: Clinical Neurology, (1 Aug 2002) Vol. 42, No. 8, pp. 757-760.
Refs: 20
ISSN: 0009-918X CODEN: RISHDJ
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
ENTRY DATE: Entered STN: 10 Apr 2003
Last Updated on STN: 10 Apr 2003

AB A male patient with juvenile parkinsonism having been treated with pergolide developed pleural effusion. Treatment of pergolide started when the patient was 49. And the symptom appeared 11 years later. The patient had no history of heart disease, chronic cough, or lung tuberculosis. His medications included pergolide 1,000 µg/ day for the past 7 years. Pergolide had been used since 1990 at the maximum dosage of 2,250

µg/day. Chest radiogram showed pleural effusion in the right lung. Parenchymal changes and thickened pleura were observed in the left lung. CT scan of the chest showed encapsulated pleural effusion and atelectasis in the mid and lower zones of the right lung. Interstitial fibrosis and pleural thickening were observed in the left lung. Pleuropulmonary changes are rare adverse effects of pergolide treatment, although they were described in other dopamine agonists such as bromocriptine. The author recommends that patients with parkinsonism who receive pergolide treatment should be regularly monitored for the development of pleuropulmonary complications.

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STN DUPLICATE 8

ACCESSION NUMBER: 2002:502876 BIOSIS
DOCUMENT NUMBER: PREV200200502876
TITLE: Pergolide: A useful agonist for the treatment of
Parkinson's disease.
Original Title: Le pergolide: Un agoniste utile dans le
traitement de la maladie de Parkinson.
AUTHOR(S): Bonnet, A.-M. [Reprint author]; Houeto, J.-L.
CORPORATE SOURCE: Federation de Neurologie, INSERM U289, Hopital
Pitie-Salpetriere, 47 Bd de L'Hopital, 75651, Paris Cedex
13, France
SOURCE: Revue Neurologique (Paris), (Juillet, 2002) Vol.
158, No. 6-7, pp. 744-745. print.
CODEN: RENEAM. ISSN: 0035-3787.
DOCUMENT TYPE: Article
LANGUAGE: French
ENTRY DATE: Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002

AB The efficiency of pergolide has been confirmed by the study of a group 29 parkinsonian patients. They were relatively young, and the duration of evolution of their Parkinson's disease was more than ten years, with levodopa-induced dyskinesia and fluctuations. In this group of patients with most serious motor disability, it has been possible to improve dyskinesia and fluctuations with a relatively important dosage of pergolide and without increase of levodopa dosage.

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STN DUPLICATE 9

ACCESSION NUMBER: 2002:437975 BIOSIS
DOCUMENT NUMBER: PREV200200437975
TITLE: Pergolide protects dopaminergic neurons in primary culture under stress conditions.
AUTHOR(S): Gille, G. [Reprint author]; Rausch, W.-D.; Hung, S.-T.; Moldzio, R.; Janetzky, B.; Hundemer, H. P.; Kolter, T.; Reichmann, H.
CORPORATE SOURCE: Department of Neurology, Technical University of Dresden, Fetscherstrasse 74, D-01307, Dresden, Germany
gabigille@yahoo.com
SOURCE: Journal of Neural Transmission, (May, 2002) Vol. 109, No. 5-6, pp. 633-643. print.
CODEN: JNGSE8. ISSN: 0300-9564.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Aug 2002
Last Updated on STN: 14 Aug 2002

AB Dopamine agonists are an important therapeutic strategy in the treatment of Parkinson's disease. They postpone the necessity for and reduce the required dose of L-3,4-dihydroxyphenylalanine (L-DOPA) medication thus protecting against the development of motor complications

and potential oxidative stress due to L-DOPA metabolism. In primary cultures from mouse mesencephalon we show that pergolide, a preferential D2 agonist enhanced the survival of healthy dopaminergic neurons at low concentrations of 0.001 μ M. About 100 fold higher concentrations (0.1 μ M) were necessary to partially reverse the toxic effects of 10 μ M 1-methyl-4-phenylpyridinium (MPP+). Pergolide was equally effective in preventing the reduction of dopamine uptake induced by 200 μ M L-DOPA. Furthermore, between 0.001-0.1 μ M it also reduced lactate production thus promoting aerobic metabolism. The present findings suggest that pergolide protects dopaminergic neurons under conditions of elevated oxidative stress.

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ACCESSION NUMBER: 2002328044 EMBASE
 TITLE: [The evolution of use of anti-Parkinson drugs in Spain]. Evolucion del consumo de farmacos antiparkinsonianos en Espana.
 AUTHOR: Montane, E.; Vallano, A., Dr. (correspondence); Castel, J.M.
 CORPORATE SOURCE: Servicio de Farmacologia Clinica, Hospital Universitario Vall d'Hebron, Passeig de la Vall d'Hebron, 119-129 E-08035 Barcelona, Spain. tv@icf.uab.es
 SOURCE: Revista de Neurologia, (1 Apr 2002) Vol. 34, No. 7, pp. 612-617.
 Refs: 43
 ISSN: 0210-0010 CODEN: RVNRAA
 COUNTRY: Spain
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 036 Health Policy, Economics and Management
 037 Drug Literature Index
 008 Neurology and Neurosurgery
 LANGUAGE: Spanish; Castilian
 SUMMARY LANGUAGE: English; Spanish; Castilian; Portuguese
 ENTRY DATE: Entered STN: 3 Oct 2002
 Last Updated on STN: 3 Oct 2002

AB Introduction. In recent years new anti-Parkinson drugs have been marketed and there has been controversy over the safety of some drugs. Objective. To analyze the evolution of the consumption of anti-Parkinson drugs and the effect of the newer drugs. Patients and methods. A study of the consumption of anti-Parkinson drugs (1989-1998). Data were obtained from the ECOM database of the Ministry of Health and TEMPUS of the National Statistics Institute. The drugs were classified using the Anatomic-Therapeutic-Clinical Classification (ATC). Consumption was expressed in defined daily dosage (DDD) and the costs in euros (€). The drugs marketed since 1990 were classified as new drugs and the others as classical drugs. Results. The total consumption of drugs increased from 1.92 DDD/1,000 inhabitants/day in 1989 to 3.64 DDD/1,000 inhabitants/day in 1998. The drugs showing the greatest increase were selegiline, pergolide and levodopa. The total pharmaceutical expenses tripled. There was a smaller increase in the consumption of new drugs (1.2% of the total in 1991 and 6.6% in 1998) than in their costs (6.7% of the total in 1991 and 38.8% in 1998). The cost per DDD of the new drugs increased five times (1989: 2.55€ and 1998: 13.59€) and that of the classical drugs was similar (1989: 0.54€ and 1998: 0.62€). Conclusions. The total consumption of anti-Parkinson drugs has progressively increased. The consumption of selegiline has also increased in spite of controversy over its safety. The new drugs have a major economic effect.

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ACCESSION NUMBER: 2002:354397 BIOSIS
DOCUMENT NUMBER: PREV200200354397
TITLE: Effects of pharmacological agents upon a transgenic model of Parkinson's Disease in *Drosophila melanogaster*.
AUTHOR(S): Pendleton, Robert G. [Reprint author]; Parvez, Feroz [Reprint author]; Sayed, Marwa [Reprint author]; Hillman, Ralph [Reprint author]
CORPORATE SOURCE: Temple University, 1900 North 12th Street, Philadelphia, PA, 19122, USA
SOURCE: FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A567. print.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jun 2002
Last Updated on STN: 26 Jun 2002

AB The human gene that codes for the protein alphasynuclein has been transferred into the *Drosophila* genome. We tested the locomotor response of these transgenic flies to prototypes of the major classes of drugs currently used to treat Parkinson's Disease (PD). A climbing or negative geotaxis assay in which the ability of the organisms to climb up the walls of a plastic vial was utilized. Normal and transgenic flies were treated with each of the drugs in their food at 1mM for 13 days and then assayed. The activity of transgenic flies treated with L-DOPA was restored to normal. The dopamine D2 agonists pergolide and bromocriptine as well as the D1 agonist SKF 38393 were substantially active. Atropine was also effective but to a lesser extent than the other antiparkinson compounds. This study demonstrates the utility of this model in studying PD and reinforces the new concepts that inhibition of the action of alphasynuclein may be useful in its treatment as may dopamine D1 receptor agonists.

L9 ANSWER 13 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 11

ACCESSION NUMBER: 2002:710478 CAPLUS
DOCUMENT NUMBER: 138:280558
TITLE: Sustained dopamine agonism with cabergoline in Parkinson's disease: evolution of therapy from animal models to man
AUTHOR(S): Appiah-Kubi, Linda S.; Chaudhuri, K. Ray
CORPORATE SOURCE: Guy's King's & St Thomas' Medical School, London, UK
SOURCE: Advances in Behavioral Biology (2002), 51(Mapping the Progress of Alzheimer's and Parkinson's Disease), 379-384
CODEN: ADBBBW; ISSN: 0099-6246
PUBLISHER: Plenum Publishing Corp.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Cabergoline [1-[(6-allylergolin-8 β -yl)carbonyl]-1-[3-(dimethylamino)propyl]-3-ethylurea] is an ergoline dopamine agonist with a high affinity for the dopamine D2 receptor. Cabergoline is unique among other available dopamine agonists as it has the longest mean elimination half life of 65-110 h calculated on the basis of urinary excretion rates in healthy volunteers and Parkinson's disease (PD) patients. Cabergoline has high selectivity for dopamine receptors, in vitro and in vivo, and binds mainly to D2 receptors in vitro and to D1 receptors with affinity similar to pergolide and 3.6 times greater than bromocriptine. Owing to its long half life, in clin. practice, cabergoline need only be given once a day, in comparison to other agonists

which usually require three times-a-day dosing. The long duration of action of cabergoline and the resultant sustained rather than pulsatile dopamine receptor stimulation in PD, is of interest given the possible role of pulsatile dopaminergic therapy in the development of dyskinesias. This review focuses on work with cabergoline in animal models and man related to its beneficial therapeutic effects in PD.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ACCESSION NUMBER: 2003009468 EMBASE

TITLE: Open-label and non-randomized study of therapeutic effect of Parkinson's disease with madopar monotherapy and concomitant madopar therapy with dopamine agonists.

AUTHOR: Qin, Bin (correspondence); Zeng, Xiangyu; Jiang, Yuping

CORPORATE SOURCE: Department of Neurology, Beijing Hospital, Beijing 100730, China.

SOURCE: Chinese Journal of Neurology, (25 Oct 2002) Vol. 35, No. 5, pp. 286-289.

Refs: 13

ISSN: 1006-7876 CODEN: ZSZAFN

COUNTRY: China

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery

LANGUAGE: Chinese

SUMMARY LANGUAGE: English; Chinese

ENTRY DATE: Entered STN: 16 Jan 2003

Last Updated on STN: 16 Jan 2003

AB Objective The clinical efficacy and safety of L-dopa monotherapy and concomitant L-dopa therapy with dopamine agonists (bromocriptine or pergolide) of the treatment of Parkinson's disease. Methods The clinical trial was performed in the multicentre, open-label study. L-dopa group: 47 cases, L-dopa plus bromocriptine group: 43 cases and L-dopa plus pergolide group: 48 cases. The clinical efficacy was assessed with modified Webster's scale and motor dysfunction rating scale for Parkinson's disease (MDRSPD), and safety data included blood hepatic and renal function tests, blood and urine routine tests, arterial blood pressure, heart rate measurements and electrocardiogram were also analyzed at the beginning and end of study. The average daily dose of L-dopa in levedopa group was (523.3 ± 235.9) mg, The average daily dose of L-dopa and bromocriptine were (526.7 ± 241.3) mg and (7.3 ± 1.5) mg in L-dopa plus bromocriptine group, respectively. The average daily dose of L-dopa and pergolide were (558.3 ± 192.9) mg and (0.235 ± 0.045) mg in L-dopa plus pergolide group separately. Result The clinical improvement was about 74.5% both in assessment of modified Webster's scale and MDRSPD in L-dopa group. The clinical score was improved in 69.8% (Webster's scale) and 79.1% (MDRSPD) in L-dopa plus bromocriptine group, respectively. The clinical improved rates were 77.9% (Webster's scale) and 81.3% (MDRSPD) in L-dopa plus bergolide group. The incidence rates of side effects were 27.7% in L-dopa group, 39.5% in L-dopa plus bromocriptine and 18.8% in L-dopa plus pergolide groups. Conclusion There was an efficacy in treatment of Parkinson's disease in either L-dopa monotherapy or combination with bromocriptine or pergolide. The treatment of L-dopa alone was more effective in the early stage of Parkinson's disease and concomitant L-dopa therapy with dopamine agonists were more effective in the advanced stage of Parkinson's disease, pergolide was not only more effective, safe and tolerable, but also fewer adverse events than Bromocriptine was in this short-term trial.

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ACCESSION NUMBER: 2002227154 EMBASE
TITLE: Pergolide-associated 'sleep attacks' in a patient with restless legs syndrome.
AUTHOR: Bassetti, Claudio (correspondence)
CORPORATE SOURCE: Neurologische Poliklinik, Universitatsspital, Frauenklinikstrasse 26, 8091 Zurich, Switzerland. claudio.bassetti@nos.usz.ch
AUTHOR: Clavadetscher, Sandra; Hess, Christian W.
CORPORATE SOURCE: Department of Neurology, University Hospital, Inselspital, Bern, Switzerland.
AUTHOR: Gugger, Matthias
CORPORATE SOURCE: Division of Pneumology, University Hospital, Inselspital, Bern, Switzerland.
SOURCE: Sleep Medicine, (2002) Vol. 3, No. 3, pp. 275-277.
Refs: 6
ISSN: 1389-9457 CODEN: SMLEAB
PUBLISHER IDENT.: S 1389-9457(01)00132-0
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jul 2002
Last Updated on STN: 11 Jul 2002

AB The occurrence of irresistible sleep episodes ('sleep attacks') has been noted in patients with Parkinson's syndrome treated with dopaagonists. This is the first report of 'sleep attacks' in a patient with restless legs syndrome in whom treatment with pergolide was reduced from 2 to less than 1 mg/day. 'Sleep attacks' were accompanied by a reduced mean sleep latency of 5 min and 20 s (without sleep onset REM periods) on a multiple sleep latency test. 'Sleep attacks' disappeared when pergolide was tapered off and substituted with pramipexol. The appearance of 'sleep attacks' as a 'withdrawal' effect of pergolide is consistent with a wakefulness-promoting action of postsynaptic dopaminergic receptors at higher doses of dopamine agonists. .COPYRGT. 2002 Published by Elsevier Science B.V.

L9 ANSWER 16 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 13

ACCESSION NUMBER: 2002:450602 CAPLUS
DOCUMENT NUMBER: 137:56883
TITLE: Clinical pharmacokinetic and pharmacodynamic properties of drugs used in the treatment of Parkinson's disease
AUTHOR(S): Deleu, Dirk; Northway, Margaret G.; Hanssens, Yolande
CORPORATE SOURCE: College of Medicine, Sultan Qaboos University, Al Khod, Oman
SOURCE: Clinical Pharmacokinetics (2002), 41(4), 261-309
CODEN: CPKNDH; ISSN: 0312-5963
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Current research in Parkinson's disease (PD) focuses on symptomatic therapy and neuroprotective interventions. Drugs that have been used for symptomatic therapy are levodopa, usually combined with a peripheral decarboxylase inhibitor, synthetic dopamine receptor agonists,

centrally-acting antimuscarinic drugs, amantadine, monoamine oxidase-B (MAO-B) inhibitors and catechol-O-methyltransferase (COMT) inhibitors. Drugs for which there is at least some evidence for neuroprotective effect are certain dopamine agonists, amantadine and MAO-B inhibitors (selegiline). Levodopa remains the most effective drug for the treatment of PD. Several factors contribute to the complex clin. pharmacokinetics of levodopa: erratic absorption, short half-life, peripheral O-methylation and facilitated transport across the blood-brain barrier. In patients with response fluctuations to levodopa, the concentration-effect curve becomes steeper and shifts to the right compared with patients with stable response. Pharmacokinetic-pharmacodynamic modeling can affect decisions regarding therapeutic strategies. The dopamine agonists include ergot derivs. (bromocriptine, pergolide, lisuride and cabergoline), non-ergoline derivs. (pramipexole, ropinirole and piribedil) and apomorphine. Most dopamine agonists have their specific pharmacol. profile. They are used in monotherapy and as an adjunct to levodopa in early and advanced PD. Few pharmacokinetic and pharmacodynamic data are available regarding centrally acting antimuscarinic drugs. They are characterized by rapid absorption after oral intake, large volume of distribution and low clearance relative to hepatic blood flow, with extensive metabolism. The mechanism of action of amantadine remains elusive. It is well absorbed and widely distributed. Since elimination is primarily by renal clearance, accumulation of the drug can occur in patients with renal dysfunction and dosage reduction must be envisaged. The COMT inhibitors entacapone and tolcapone dose-dependently inhibit the formation of the major metabolite of levodopa, 3-O-methyldopa, and improve the bioavailability and reduce the clearance of levodopa without significantly affecting its absorption. They are useful adjuncts to levodopa in patients with end-of-dose fluctuations. The MAO-B inhibitor selegiline may have a dual effect: reducing the catabolism of dopamine and limiting the formation of neurotoxic free radicals. The pharmacokinetics of selegiline are highly variable; it has low bioavailability and large volume of distribution. The oral clearance is many-fold higher than the hepatic blood flow and the drug is extensively metabolized into several metabolites, some of them being active. Despite the introduction of several new drugs to the antiparkinsonian armamentarium, no single best treatment exists for an individual patient with PD. Particularly in the advanced stage of the disease, treatment should be individually tailored.

OS.CITING REF COUNT: 66 THERE ARE 66 CAPLUS RECORDS THAT CITE THIS
RECORD (66 CITINGS)
REFERENCE COUNT: 303 THERE ARE 303 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

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ACCESSION NUMBER: 2003021018 EMBASE
TITLE: An evidence-based review of dopamine receptor agonists in
the treatment of Parkinson's disease.
AUTHOR: Deleu, Dirk, Dr. (correspondence)
CORPORATE SOURCE: College of Medicine, Sultan Qaboos University, PO Box 35,
Al Khod, PC-123, Oman. dtodeleu@squ.edu.om
AUTHOR: Northway, Margaret G.; Hanssens, Yolande
SOURCE: Neurosciences, (Oct 2002) Vol. 7, No. 4, pp.
221-231.
Refs: 98
ISSN: 1319-6138 CODEN: NRSABF
COUNTRY: Saudi Arabia
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index

038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Jan 2003
Last Updated on STN: 29 Jan 2003

AB Apomorphine and certain ergot alkaloids (bromocriptine, lisuride and pergolide) have been available for several decades; for the last few years, they were joined by newer dopamine agonists (cabergoline, pramipexole and ropinirole) most of them are non-ergolines. Each of these dopamine agonists has its own pharmacological characteristics and occupies a place in the pharmacotherapy of Parkinson's disease. In this evidence-based review, emphasis is put on the clinical efficacy of dopamine agonists in early and advanced Parkinson's disease, and where possible comparative evidence regarding their efficacy and safety is provided. In addition, their clinical pharmacokinetics, adverse effect profiles and most relevant interactions will be summarized.

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ACCESSION NUMBER: 2002229378 EMBASE
TITLE: Frontiers in neuropharmacotherapy part II: Multiple sclerosis and Parkinson's disease.
AUTHOR: Chappell, Jill C.; Cohen, Henry (correspondence)
CORPORATE SOURCE: A. and M. Schwartz Coll. of Pharmacy, Long Island University, 75 DeKalb Avenue, Brooklyn, NY 11201-5407, United States. hcohenliu@aol.com
SOURCE: Journal of Pharmacy Practice, (2002) Vol. 15, No. 3, pp. 221-240.
Refs: 66
ISSN: 0897-1900 CODEN: JPPREU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
039 Pharmacy
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jul 2002
Last Updated on STN: 11 Jul 2002

AB Disease-modifying agents such as β -interferons and glatiramer acetate have a significant impact on slowing the course of relapsing-remitting multiple sclerosis (MS). Therapeutic guidelines recommend initiating therapy with 1 of the 3 agents shortly after diagnosis of clinically definite MS, but there is insufficient data to specifically select one of the therapies. New research helps differentiate the therapies based on their induction of neutralizing antibodies, optimal dosing, and monitoring strategies. New treatments for secondary progressive MS are also emerging with evidence for the use of interferon β -1b and the approval of mitoxantrone. Future therapies for MS include oral glatiramer acetate and combination therapy. Levodopa continues to be the standard of care for the treatment of Parkinson's disease, but the approval of newer therapies that spare the use of levodopa and improve safety profiles are changing the management of the disease. Dopamine agonists such as bromocriptine and pergolide have been used to manage complications of levodopa therapy in patients with advanced disease, but new research supports the use of the more selective dopamine agonists, pramipexole and ropinirole, as monotherapy in early Parkinson's disease. The combination of a catechol-O-methyltransferase (COMT) inhibitor with levodopa provides a new therapeutic option for treating patients with motor complications in advanced disease.

L9 ANSWER 19 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 15

ACCESSION NUMBER: 2002:728121 CAPLUS
DOCUMENT NUMBER: 137:257140
TITLE: Choosing the right dopamine agonist for patients with Parkinson's disease
AUTHOR(S): Lebrun-Frenay, C.; Borg, M.
CORPORATE SOURCE: Department of Neurology, University of Nice, Fr.
SOURCE: Current Medical Research and Opinion (2002), 18(4), 209-214
CODEN: CMROCX; ISSN: 0300-7995
PUBLISHER: LibraPharm Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Dopamine receptor agonists (DA) are assuming an increasing importance in the treatment of both early and advanced symptoms of Parkinson's disease (PD). However, choosing the right DA for patients with PD unfortunately remains more a pragmatic medical art than a science. The aim of this review is to provide a realistic point of view on the strengths and weaknesses of five DAs: bromocriptine, ropinirole, pergolide, pramipexole and piribedil. This has been done by analyzing their resp.: (1) flexibility in PD, i.e. in monotherapy, in early and in late combination with levodopa; (2) safety profile and (3) titration schedule. These five DAs are not evenly matched regarding these three criteria. The differences observed highlight the therapeutic value of piribedil, which has a flexible indication, adapted to all stages of PD, a safer profile and the most simple initiation schedule.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 20 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:277653 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 39-16997
TITLE: Choosing the right dopamine agonist for patients with Parkinson's disease
AUTHOR(S): Lebrun-Frenay, C; Borg, M
CORPORATE SOURCE: Reprints: Hop Louis Pasteur, Serv Neurol, 30 Voie Romaine,BP 69, F-06002 Nice, France
christine.lebrun-frenay@wanadoo.fr; Univ Nice, Dept Neurol, Nice, France
SOURCE: Current Medical Research and Opinion (England), (2002) Vol. 18, pp. 209-214. 45 Refs.
CODEN: CMROCX. ISSN: 0300-7995.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 2002:16977
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 2002
Last Updated on STN: 10 Dec 2002

AB Dopamine receptor agonists (DA) are assuming an increasing importance in the treatment of both early and advanced symptoms of Parkinson's disease (PD). However, choosing the right DA for patients with PD unfortunately remains more a pragmatic medical art than a science. The aim of this review is to provide a realistic point of view on the strengths and weaknesses of five DAs: bromocriptine, ropinirole, pergolide, pramipexole and piribedil. This has been done by analysing their respective: (1) flexibility in PD, i.e. in monotherapy, in early and in late combination with levodopa; (2) safety profile and (3) titration schedule. These five DAs are not evenly matched regarding these three criteria. The differences observed highlight the therapeutic value

of piribedil, which has a flexible indication, adapted to all stages of PD, a safer profile and the most simple initiation schedule.

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L11 48 L9 AND (SELEGILINE/AB)

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L11 ANSWER 1 OF 48 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:260796 BIOSIS
DOCUMENT NUMBER: PREV200200260796
TITLE: Rapid-eye-movement sleep disorders in Parkinson's disease.
Original Title: Les troubles du sommeil paradoxal dans la
maladie de Parkinson.
AUTHOR(S): Gagnon, J.-F.; Montplaisir, J.; Bedard, M.-A. [Reprint
author]
CORPORATE SOURCE: Unite des Troubles du Mouvement Andre Barbeau, Hotel-Dieu,
CHUM, 3840, rue St-Urbain, Montreal, Quebec, H2W 1T8,
Canada
bedard.marc-andre@uqam.ca
SOURCE: Revue Neurologique (Paris), (Fevrier, 2002) Vol.
158, No. 2, pp. 135-152. print.
CODEN: RENEAM. ISSN: 0035-3787.
DOCUMENT TYPE: Article
LANGUAGE: French
ENTRY DATE: Entered STN: 24 Apr 2002
Last Updated on STN: 24 Apr 2002

AB During the past 10 years, there has been an increasing interest in the study of rapid-eye-movement (REM) sleep in neurodegenerative diseases and more particularly in Parkinson's disease (PD). This interest is justified by the strong association observed between these diseases and REM sleep behavior disorder (RBD). In the first section of this paper, a critical review of the literature on the presence of REM sleep disorders in PD is presented. Studies that show an association between PD and RBD are reviewed. Studies that report the presence of other REM sleep disorders in PD (short latency, abnormal length and/or proportion of REM sleep, increasing occurrence of hallucinations) are then discussed. Limitations of the criteria proposed by Rechtschaffen et Kales (1968) for the quantification of REM sleep are also presented. Some authors believe that dopaminergic (DA) agents used in the treatment of PD (levodopa, bromocriptine, pergolide, pramipexole and selegiline)

could be a responsible factor for the occurrence of REM sleep disorders observed in this disease. The literature concerning the impact of these DA agents on human REM sleep is therefore critically reviewed. It is concluded that DA agents cannot explain on their own the presence of REM sleep disorders in PD. Other causes, among which the disturbance of some neurochemical systems linked to the neuropathological process of the disease, must be considered in order to explain these REM sleep disorders. In the second section of this paper, we present the different pathophysiological hypotheses proposed to explain REM sleep disorders in PD, such as a dysfunction of the cholinergic, noradrenergic, serotonergic, dopaminergic or GABAergic neurons. Emphasis is placed on the role of cholinergic neurons of the pedunculopontine and laterodorsal tegmental nuclei, structures shown to be particularly impaired in PD. Neurophysiological, neuroanatomical and neuropharmacological studies demonstrate that these neurons are strongly implicated in the different REM sleep parameters (muscular atonia, electroencephalographic desynchronisation, ponto-geniculo-occipital spikes). Finally, future research directions are proposed.

L11 ANSWER 2 OF 48 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:261686 BIOSIS
DOCUMENT NUMBER: PREV200100261686
TITLE: Iron chelating, antioxidant and cytoprotective properties of dopamine receptor agonist; apomorphine.
AUTHOR(S): Youdim, M. B. H. [Reprint author]; Gassen, M.; Gross, A.; Mandel, S.; Grunblatt, E.
CORPORATE SOURCE: Department of Pharmacology, Faculty of Medicine, Eve Topf and National Parkinson's Foundation Centers, Technion, Haifa, Israel
youdim@tx.technion.ac.il
SOURCE: Journal of Neural Transmission Supplement, (2000)
Vol. 58, pp. 83-96. print.
CODEN: JNTSD4. ISSN: 0303-6995.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 30 May 2001
Last Updated on STN: 19 Feb 2002

AB There have been many attempts to discover neuroprotective drugs for the treatment of Parkinson's disease (PD). Many of these compounds either do not cross the blood brain barrier or are not very effective in the 6-hydroxydopamine or MPTP (N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) models of PD. We have examined several compounds including dopamine receptor agonist bromocriptine, lisuride, pergolide and R-apomorphine for their neuroprotective action against the above neurotoxins in PC12 and dopamine neuroblastoma cell lines in culture and in vivo. R-apomorphine exhibited relatively potent neuroprotective action in vitro, cell culture and in vivo as a radical scavenger and iron chelator, because of its catechol structure. The recent clinical trials with apomorphine, where parkinsonian subjects can be weaned off L-dopa would suggest that this drug either exerts a neuroprotective action or that continuous sustained stimulation of dopamine receptor may be responsible for its unusual pharmacological activity. Apomorphine has a far more broad neuroprotective activity in the various models as compared with l-selegiline and may therefore be an ideal drug to study neuroprotection in parkinsonian subjects with the use of PET or SPECT.

L11 ANSWER 3 OF 48 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:542644 BIOSIS
DOCUMENT NUMBER: PREV200000542644
TITLE: Pre-clinical studies of pramipexole: Clinical relevance.
AUTHOR(S): Hubble, J. P. [Reprint author]

CORPORATE SOURCE: Department of Neurology, The Ohio State University
Parkinson's Disease Center, 1581 Dodd Drive, Suite 371,
Columbus, OH, 43210, USA

SOURCE: European Journal of Neurology, (May, 2000) Vol.
7, No. Supplement 1, pp. 15-20. print.
ISSN: 1351-5101.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 13 Dec 2000

Last Updated on STN: 11 Jan 2002

AB This paper reviews the preclinical study of the novel dopamine agonist pramipexole and its use in early Parkinson's disease (PD). Emphasis will be given to those properties distinguishing this drug from other dopamine agonists, the relevance of the preclinical data to clinical trial results in early PD, and the putative neuroprotective properties of the compound. The conventional dopamine agonists are ergot-derived compounds that are most widely used as adjunctive therapies in advancing Parkinson's disease (PD). Examples of conventional agonists are bromocriptine and pergolide. Pramipexole is an aminobenzothiazole compound, recently introduced for the treatment of both early and advanced PD. Its nonergot structure may reduce the risk of side-effects, considered unique to ergot drugs, such as membranous fibrosis. Pramipexole is a full dopamine agonist with high selectivity for the D2 dopamine receptor family. This family includes the D2, D3 and D4 receptor subtypes. Pramipexole has a 5- to 7-fold greater affinity for the D3 receptor subtype with lower affinities for the D2 and D4 receptor subtypes. The drug has only minimal α 2-adrenoceptor activity and virtually no other receptor agonism or antagonism. The optimal dopamine receptor activation for the safe and effective treatment of PD is not known. Findings in animal models and clinical studies indicate that activation of the postsynaptic D2 receptor subtype provides the most robust symptomatic improvement in PD. Given its pharmacological profile, it is not surprising that pramipexole was found to be effective in ameliorating parkinsonian signs in animal models. This therapeutic effect has been confirmed in clinical trials in both early and advanced PD. In early disease, it provides a clear reduction in the chief motor manifestations of PD and improved activities of daily living. Perhaps most striking is the large number of clinical trial patients who have remained on pramipexole monotherapy for many months. The majority of these subjects have been maintained on pramipexole for an excess of 24 months without requiring additional symptomatic treatment with levodopa. This is in contrast to the general clinical experience with older conventional agonists. Pramipexole also has a favourable pharmacokinetic profile. It is rapidly absorbed with peak levels appearing in the bloodstream within 2 h of oral dosing. It has a high absolute bioavailability of > 90% and can be administered without regard to meals. It has no significant effects on other antiparkinson drugs such as levodopa or selegiline. Its excretion is primarily renal and, thus, has little or no impact on hepatic cytochrome P450 enzymes or other related metabolic pathways. Pramipexole has also been theorized to have 'neuroprotectant' properties. Oxyradical generation is posited as a cause or accelerant of brain nigral cell death in PD. Pramipexole stimulates brain dopamine autoreceptors and reduces dopamine synthesis and turnover which may minimize oxidative stress due to dopamine metabolism. Furthermore, the compound has a low oxidation potential that may serve as an oxyradical scavenger in the PD brain. In summary, pramipexole is a new antiparkinson medication found to have unique dopamine agonist characteristics and putative neuroprotective properties.

TITLE: Drug therapy for Parkinson's disease.
AUTHOR(S): Charles, P. David [Reprint author]; Davis, Thomas L.
CORPORATE SOURCE: 352 MCS, 2100 Pierce Ave., Nashville, TN 37212, USA
SOURCE: Southern Medical Journal, (1996) Vol. 89, No. 9,
pp. 851-856.
CODEN: SMJOAV. ISSN: 0038-4348.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Oct 1996
Last Updated on STN: 24 Oct 1996

AB Parkinson's disease (PD) is a common neurodegenerative disease characterized by tremor, rigidity, bradykinesia, and loss of postural reflexes. Although the agents available for symptomatic treatment now allow most parkinsonian patients to live a normal life-span, these patients become progressively unable to participate in social functions, perform activities of daily living, and work. Therapy for PD may be associated with many complications that contribute to these disabilities. For this reason, education is helpful for the patient newly diagnosed with PD. Over the past 6 years, three new medications (selegiline, pergolide, and controlled-release levodopa) have been approved for use in Parkinson's disease. Other agents now available for the treatment of psychiatric illness may also be helpful in selected cases of PD. With this in mind, we review the commonly prescribed drugs and outline a rational plan for treatment of parkinsonism.

L11 ANSWER 5 OF 48 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:385106 BIOSIS
DOCUMENT NUMBER: PREV199699107462

TITLE: Treatment of early Parkinson's diseases: Are complicated strategies justified?
AUTHOR(S): Ahlskog, J. Eric
CORPORATE SOURCE: Dep. Neurology, Mayo Clinic Rochester, 200 First St. SW, Rochester, MN 55905, USA
SOURCE: Mayo Clinic Proceedings, (1996) Vol. 71, No. 7, pp. 659-670.
CODEN: MACPAJ. ISSN: 0025-6196.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Aug 1996
Last Updated on STN: 26 Aug 1996

AB A variety of medical treatment strategies have been proposed as a means of slowing the progression of Parkinson's disease. This includes administration of selegiline (deprenyl) therapy, early use of bromocriptine or pergolide, and delay of levodopa therapy or restriction of the dose. There is no compelling evidence supporting the use of any of these treatment strategies for this purpose. Carbidopa-levodopa remains the most potent medication for symptomatic treatment of Parkinson's disease. Although starting levodopa therapy with the controlled-release formulation is advocated, this does not appear to have any major advantages over standard carbidopa-levodopa. Further studies are needed to identify other means of halting the progression of Parkinson's disease.

L11 ANSWER 6 OF 48 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:415059 BIOSIS
DOCUMENT NUMBER: PREV199598429359

TITLE: The Therapeutic Potential of Moclobemide, a Reversible Selective Monoamine Oxidase A Inhibitor in Parkinson's disease.
AUTHOR(S): Sieradzan, Katarzyna [Reprint author]; Channon, Shelley; Ramponi, Cristina; Stern, Gerald M.; Lees, Andrew J.;

Youdim, Moussa B. H.
CORPORATE SOURCE: Dep. Neurol., Manchester Royal Infirmary, Oxford Road,
Manchester, M13, UK
SOURCE: Journal of Clinical Psychopharmacology, (1995)
Vol. 15, No. 4 SUPPL. 2, pp. 51S-59S.
CODEN: JCPYDR. ISSN: 0271-0749.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Sep 1995
Last Updated on STN: 27 Sep 1995

AB Dopamine is equally well deaminated oxidatively by monoamine oxidase (MAO) A and B types. Selegiline (L-deprenyl), a selective inhibitor of MAO-B, ameliorates the "wearing off" akinesia and delays the need for levodopa in mild, previously untreated Parkinson's disease. The therapeutic potential of selective inhibition of MAO-A in Parkinson's disease has not been examined in detail. MAO-A accounts for only about 20% of total MAO activity in the human basal ganglia, and it differs from MAO-B in distribution. In contrast to MAO-B, which is confined to the extraneuronal compartment, MAO-A is found both extraneuronally and within the presynaptic dopaminergic terminals. The inhibition of MAO-A might alter the intraneuronal handling of dopamine reuptaken from synaptic clefts and thereby prolong oral levodopa benefit. We have given moclobemide, a selective, reversible inhibitor of MAO-A, to nondepressed patients with Parkinson's disease receiving standard levodopa/peripheral decarboxylase inhibitor or levodopa with dopaminergic agonist (bromocriptine, pergolide). Selegiline was discontinued at least 8 weeks earlier. A standard oral levodopa challenge was performed at the patient's entry to the study and repeated on the 22nd day of moclobemide treatment (150 mg thrice daily). The overall time spent "on" and "off" before the onset of treatment and during the last week on the drug was estimated from the patients' diaries. Neuropsychological assessments were also made before and after 3 weeks of moclobemide to measure possible effects on cognitive performance and mood. In acute levodopa challenge, the latency of motor response was significantly shortened and its duration was prolonged during moclobemide treatment. Similarly, the Webster's scores in "off" state after overnight withdrawal of dopaminergic medication improved on moclobemide. In nondepressed parkinsonian patients, moclobemide did not alter mood and cognitive measures. The mild symptomatic effect and good tolerance with standard therapy suggest that moclobemide may be a particularly useful antidepressant in Parkinson's disease.

L11 ANSWER 7 OF 48 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:83090 BIOSIS
DOCUMENT NUMBER: PREV199598097390
TITLE: Early idiopathic parkinsonism: Initiation and optimization of treatment.
AUTHOR(S): Calne, Donald B.
CORPORATE SOURCE: Neurodegenerative Disorders Cent., Faculty Med., Vancouver Hosp., Purdy Pavillion, 2211 Wesbrook Mall, Vancouver, BC V6T 2B5, Canada
SOURCE: Clinical Neuropharmacology, (1994) Vol. 17, No. SUPPL. 2, pp. S14-S18.
CODEN: CLNEDB. ISSN: 0362-5664.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Feb 1995
Last Updated on STN: 23 Feb 1995

AB Once a diagnosis of idiopathic parkinsonism has been made, the choice and timing of therapy depend almost entirely on the patient's need for symptomatic relief, as no presently available therapy has any effect on the pathogenesis of the disease. Five categories of drugs are

available for the treatment of idiopathic parkinsonism. Anticholinergic agents are effective against tremor but have prominent adverse effects. Amantadine has similar effects but is more active against rigidity and bradykinesia. Selegiline is a monoamine oxidase-B inhibitor: once thought to affect the pathogenesis of idiopathic parkinsonism, it is now known to offer only symptomatic relief. The dopamine agonists (bromocriptine, pergolide, and lisuride) stimulate D-2 receptors: they have antiparkinsonian effects and tolerance profiles broadly similar to those of levodopa but are slightly less efficacious. Pleural effusions and pulmonary fibrosis are unusual but important complication, of these drugs: chest x-ray examinations are therefore recommended for all patients starting such treatment. Levodopa (combined with an extracerebral decarboxylase inhibitor to prevent nausea, the main adverse effect) has become the standard antiparkinsonism treatment. Patients using this preparation can suffer considerable variations in mobility and dyskinesia, which may be related to rapid, large-scale oscillations in plasma levodopa concentrations. Controlled-release (CR) preparations have been developed in an attempt to minimize these fluctuations and reduce long-term side effects. There is no universally agreed treatment for idiopathic parkinsonism. However, experience shows that a good balance of antiparkinsonian activity and adverse effects can be obtained by initiating treatment with a combination of levodopa and a decarboxylase inhibitor. A dopamine agonist can be added if the disease progresses and increased therapeutic activity is required.

L11 ANSWER 8 OF 48 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
 ACCESSION NUMBER: 1994:165810 BIOSIS
 DOCUMENT NUMBER: PREV199497178810
 TITLE: An analysis of treatment options and outcome in patients with Parkinson's disease and severe dyskinesias.
 AUTHOR(S): Mark, Margery H.,; Sage, Jacob I. [Reprint author]
 CORPORATE SOURCE: Dep. Neurol., UMDNJ-Robert Wood Johnson Med. Sch., CN-19, New Brunswick, NJ 08903, USA
 SOURCE: Annals of Clinical and Laboratory Science, (1994) Vol. 24, No. 1, pp. 12-21.
 CODEN: ACLSCP. ISSN: 0091-7370.
 DOCUMENT TYPE: Article
 LANGUAGE: English
 ENTRY DATE: Entered STN: 8 Apr 1994
 Last Updated on STN: 10 Apr 1994

AB Forty-one patients with Parkinson's disease and severe dyskinesias were analyzed retrospectively to determine if some general principles would emerge to aid physicians handling this complication of treatment. Dyskinesia type (high dopa chorea (HDC), low dopa chorea (LDC), high dopa dystonia (HDD), and low dopa dystonia (LDD)) predicted response to treatment and whether or not levodopa dose reduction would benefit dyskinesias without producing unacceptable "offs." High dopa chorea improved best but at the expense of increased "off" time, followed by LDD, HDD, and LDC. Levodopa reduction was an acceptable strategy in ameliorating HDC and LDD only. Adjunctive therapy benefitted all dyskinesia types, although the majority of patients (12/17) helped by selegiline had LDD or LDC. Generally, low doses of dopamine agonists were helpful (bromocriptine lt 20 mg/day; pergolide lt 2 mg/day). When adding adjunctive therapy (except for selegiline or controlled-release carbidopa/levodopa), concomitant reduction in daily dose of levodopa was not an effective strategy to decrease dyskinesias. Serial trials of multiple drug regimens are useful in these patients.

L11 ANSWER 9 OF 48 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
 ACCESSION NUMBER: 1992:283211 BIOSIS
 DOCUMENT NUMBER: PREV199294007861; BA94:7861

TITLE: PARKINSONISM TREATMENT PART III. UPDATE.
AUTHOR(S): COLLIER D S [Reprint author]; BERG M J; FINCHAM R W
CORPORATE SOURCE: COLLEGE PHARMACY, UNIVERSITY IOWA, IOWA CITY, IOWA 52242,
USA
SOURCE: Annals of Pharmacotherapy, (1992) Vol. 26, No. 2,
pp. 227-233.
CODEN: APHRER. ISSN: 1060-0280.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 10 Jun 1992
Last Updated on STN: 10 Jun 1992

AB Objective: The purpose of this review is to update clinicians with recent advances in the management of parkinsonism, including drug therapy, transplantation, and diet. Data sources: Pertinent articles were obtained from an English-language literature search using MEDLINE (1970-1991), Index Medicus (1987-1991), Current Contents (1990), and bibliographic reviews of review articles. Index terms included parkinsonism, selegiline, pergolide, vitamin E, and transplantation. Fifty-five articles (representing 85 percent of the complete literature search) were selected by multiple reviewers for their contribution to the stated purpose. Emphasis was placed on double-blind, placebo-controlled, and randomized studies. Data from cited articles were examined by multiple reviewers for support of their stated hypothesis and were included as background for justification of major points in this article; critical studies were abstracted in more detail. Results: New therapeutic measures have been added to the treatment of parkinsonism. Selegiline, a monoamine oxidase inhibitor type B, has shown beneficial results, especially in early stages. Pergolide, a dopamine agonist, may be an efficacious alternative to bromocriptine resistance or intolerable adverse effects. Vitamin E may have protective antioxidant properties, but very few clinical data are available. Fetal tissue transplantation needs continued research and remains very controversial. Diet modifications may maximize the results of therapy with exogenous dopamine therapy. Conclusions: Clinicians should familiarize themselves with new alternatives for the management of parkinsonism in order to be reliable consultants for both professional and lay persons.

L11 ANSWER 10 OF 48 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 1991:140709 BIOSIS
DOCUMENT NUMBER: PREV199191077249; BA91:77249
TITLE: EARLY COMBINATION OF SELEGILINE AND LOW-DOSE L DOPA AS
INITIAL SYMPTOMATIC THERAPY IN PARKINSON'S DISEASE
EXPERIENCE IN 26 PATIENTS RECEIVING COMBINED THERAPY FOR 26
MONTHS.
AUTHOR(S): ELIZAN T S [Reprint author]; MOROS D A; YAHR M D
CORPORATE SOURCE: DEP NEUROLOGY, BOX 1137, MOUNT SINAI MED CENTER, 1 GUSTAVE
L LEVY PL, NEW YORK NY 10029, USA
SOURCE: Archives of Neurology, (1991) Vol. 48, No. 1, pp.
31-34.
CODEN: ARNEAS. ISSN: 0003-9942.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 14 Mar 1991
Last Updated on STN: 22 May 1991

AB Thirty-eight patients newly diagnosed as having Parkinson's disease (mean age, 57.3 years; mean Parkinson's disease duration, 2.7 years) in the earlier phase of the disease (mean Hoehn/Yahr stage, 2; mean motor scores, 11.4) were given selegiline

(Deprenyl), 10 mg daily, and maintained on this drug alone until significant clinical worsening warranted the addition of low-dose levodopa (Sinemet, 25/100 three to four doses per day). Five of these patients were not yet receiving additional levodopa despite some worsening of motor scores. Of the 33 patients now taking combined therapy, seven have been followed up for 6 months or less. Twenty-four (92%) of the 26 patients taking combined therapy for a mean of 26 months (8.5 to 99 months) who have had Parkinson's disease for 6 years showed a dramatic improvement in their parkinsonism shortly after the addition of levodopa, with significant decreases in their rated motor scores, such improvement being maintained at their latest neurologic evaluation. Eighteen (75%) of these 24 patients responded to the combined selegiline/levodopa therapy with degrees of improvement equal to or greater than 50%, compared with their motor status at the start of combined therapy just before the addition of levodopa. This degree of "reversal" of parkinsonism on addition of levodopa (mean carbidopa/levodopa dose, 98/380 mg) was not observed in any of these same patients receiving selegiline alone for an average of 13.8 months. Four patients taking combined therapy developed mild, transient, abnormal involuntary movements, and end-of-dose pattern of response after more than 2 years of combined therapy (24.75 and 33.5 months, respectively). Our results on combined selegiline/levodopa therapy reemphasize the continuing dominant role of levodopa as the primary drug for the symptomatic treatment of Parkinson's disease. A possible synergistic role of selegiline with levodopa in the early cases is suggested by the sustained therapeutic effectiveness of even low doses of the latter for a period of 26 months, with a delay in the appearance of relatively minor side effects developing only after more than 2 years of combined therapy. At an average disease duration of 6 years, no patient has had a major functional disability. A concurrently studied control group of patients treated with low-dose levodopa alone, or one treated with a combination of low-dose levodopa and a dopamine agonist like bromocriptine or pergolide, may have clarified further the role of selegiline, but such control subjects were not available to us at this time. We suggest the early combination of a selective monoamine oxidase type B inhibitor like selegiline, and the original dopamine replacement drug, levodopa (as low-dose Sinemet), as initial symptomatic therapy in newly diagnosed cases of Parkinson's disease.

L11 ANSWER 11 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:450602 CAPLUS

DOCUMENT NUMBER: 137:56883

TITLE: Clinical pharmacokinetic and pharmacodynamic properties of drugs used in the treatment of Parkinson's disease

AUTHOR(S): Deleu, Dirk; Northway, Margaret G.; Hanssens, Yolande

CORPORATE SOURCE: College of Medicine, Sultan Qaboos University, Al Khod, Oman

SOURCE: Clinical Pharmacokinetics (2002), 41(4), 261-309

CODEN: CPKNDH; ISSN: 0312-5963

PUBLISHER: Adis International Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Current research in Parkinson's disease (PD) focuses on symptomatic therapy and neuroprotective interventions. Drugs that have been used for symptomatic therapy are levodopa, usually combined with a peripheral decarboxylase inhibitor, synthetic dopamine receptor agonists, centrally-acting antimuscarinic drugs, amantadine, monoamine oxidase-B (MAO-B) inhibitors and catechol-O-methyltransferase (COMT) inhibitors. Drugs for which there is at least some evidence for neuroprotective effect

are certain dopamine agonists, amantadine and MAO-B inhibitors (selegiline). Levodopa remains the most effective drug for the treatment of PD. Several factors contribute to the complex clin. pharmacokinetics of levodopa: erratic absorption, short half-life, peripheral O-methylation and facilitated transport across the blood-brain barrier. In patients with response fluctuations to levodopa, the concentration-effect curve becomes steeper and shifts to the right compared with patients with stable response. Pharmacokinetic-pharmacodynamic modeling can affect decisions regarding therapeutic strategies. The dopamine agonists include ergot derivs. (bromocriptine, pergolide, lisuride and cabergoline), non-ergoline derivs. (pramipexole, ropinirole and piribedil) and apomorphine. Most dopamine agonists have their specific pharmacol. profile. They are used in monotherapy and as an adjunct to levodopa in early and advanced PD. Few pharmacokinetic and pharmacodynamic data are available regarding centrally acting antimuscarinic drugs. They are characterized by rapid absorption after oral intake, large volume of distribution and low clearance relative to hepatic blood flow, with extensive metabolism. The mechanism of action of amantadine remains elusive. It is well absorbed and widely distributed. Since elimination is primarily by renal clearance, accumulation of the drug can occur in patients with renal dysfunction and dosage reduction must be envisaged. The COMT inhibitors entacapone and tolcapone dose-dependently inhibit the formation of the major metabolite of levodopa, 3-O-methyldopa, and improve the bioavailability and reduce the clearance of levodopa without significantly affecting its absorption. They are useful adjuncts to levodopa in patients with end-of-dose fluctuations. The MAO-B inhibitor selegiline may have a dual effect: reducing the catabolism of dopamine and limiting the formation of neurotoxic free radicals. The pharmacokinetics of selegiline are highly variable; it has low bioavailability and large volume of distribution. The oral clearance is many-fold higher than the hepatic blood flow and the drug is extensively metabolized into several metabolites, some of them being active. Despite the introduction of several new drugs to the antiparkinsonian armamentarium, no single best treatment exists for an individual patient with PD. Particularly in the advanced stage of the disease, treatment should be individually tailored.

OS.CITING REF COUNT: 66 THERE ARE 66 CAPLUS RECORDS THAT CITE THIS RECORD (66 CITINGS)

REFERENCE COUNT: 303 THERE ARE 303 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:49017 CAPLUS

DOCUMENT NUMBER: 135:86375

TITLE: Iron chelating, antioxidant and cytoprotective properties of dopamine receptor agonist; apomorphine

AUTHOR(S): Youdim, M. B. H.; Gassen, M.; Gross, A.; Mandel, S.; Grunblatt, E.

CORPORATE SOURCE: Department of Pharmacology, Eve Topf and National Parkinson's Foundation Centers, Bruce Rappaport Family Research Institute, Faculty of Medicine, Haifa, Israel

SOURCE: Advances in Research on Neurodegeneration (2000), 7(7th International Winter Conference on Neurodegeneration, 1999), 83-96

CODEN: ARNEFX; ISSN: 1068-719X

PUBLISHER: Springer-Verlag Wien

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 30 refs. There have been many attempts to discover neuroprotective drugs for the treatment of Parkinson's disease

(PD). Many of these compds. either do not cross the blood brain barrier or are not very effective in the 6-hydroxydopamine or MPTP (N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) models of PD. We have examined several compds. including dopamine receptor agonist bromocriptine, lisuride, pergolide and R-apomorphine for their neuroprotective action against the above neurotoxins in PC12 and dopamine neuroblastoma cell lines in culture and in vivo. R-apomorphine exhibited relatively potent neuroprotective action in vitro, cell culture and in vivo as a radical scavenger and iron chelator, because of its catechol structure. The recent clin. trials with apomorphine, where parkinsonian subjects can be weaned off L-dopa would suggest that this drug either exerts a neuroprotective action or that continuous sustained stimulation of dopamine receptor may be responsible for its unusual pharmacol. activity. Apomorphine has a far more broad neuroprotective activity in the various models as compared with l-selegiline and may therefore be an ideal drug to study neuroprotection in parkinsonian subjects with the use of PET or SPECT.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:92856 CAPLUS

DOCUMENT NUMBER: 132:117010

TITLE: Comparative tolerability of the newer generation antiparkinsonian agents

AUTHOR(S): Lambert, Dorothee; Waters, Cheryl H.

CORPORATE SOURCE: Department of Neurology, Division of Movement Disorders, University of Southern California, Los Angeles, CA, USA

SOURCE: Drugs & Aging (2000), 16(1), 55-65

CODEN: DRAGE6; ISSN: 1170-229X

PUBLISHER: Adis International Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 44 refs. In recent years, the treatment of Parkinson's disease has undergone an immense amount of research, resulting in the development of multiple new medications. This has largely been fuelled by dissatisfaction over the development of motor complications secondary to long term levodopa therapy. Different treatment approaches are applied depending on the stage of Parkinson's disease. In early and mild Parkinson's disease, selegiline offers a limited symptomatic effect. Its neuroprotective effect, although at present theor., has questionable clin. relevance. Increased mortality associated with selegiline has been reported, although a meta-anal. of 5 different trials did not support this finding. The newer, non-ergoline dopamine agonists, pramipexole and ropinirole, have undergone extensive studies to evaluate their efficacy as monotherapy in early Parkinson's disease. These newer agonists are ideal initial symptomatic medications, primarily because they delay the onset of levodopa-induced motor fluctuations. Efficacy of the newer dopamine agonists in advanced disease seems to be comparable to that of the older agents, bromocriptine and pergolide. Adverse effects can be reduced by starting the medication at a very low dose and then slowly titrating upward. Catechol-O-Me transferase (COMT) inhibitors are indicated for the treatment of motor fluctuations in advanced disease, particularly the "wearing-off" phenomenon. Tolcapone, a peripheral and central COMT inhibitor, appears to be quite effective, producing a 47% reduction in "off" time. Unfortunately, 3 deaths have been observed, which are presumably secondary to tolcapone therapy. The drug has been withdrawn in many countries, and liver enzyme testing is mandatory in the US.

Entacapone, a purely peripheral COMT inhibitor with a lower potency than tolcapone, has also proved to be effective and has not been associated with liver damage, obviating the need for testing.

OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1999:150305 CAPLUS
DOCUMENT NUMBER: 130:261327
TITLE: Ropinirole: a dopamine agonist for the treatment of Parkinson's disease
AUTHOR(S): Kuzel, Mary D.
CORPORATE SOURCE: Pharmacy Practice, College of Pharmacy, North Dakota State University, Fargo, ND, 58103, USA
SOURCE: American Journal of Health-System Pharmacy (1999), 56(3), 217-224
CODEN: AHSPEK; ISSN: 1079-2082
PUBLISHER: American Society of Health-System Pharmacists
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 42 refs. The pharmacol., pharmacokinetics, clin. efficacy, adverse effects, dosage and administration, and formulary considerations of ropinirole are reviewed. Ropinirole is a nonergoline dopamine agonist that binds to dopamine D2-receptors; the drug is indicated for use in the symptomatic treatment of early and late Parkinson's disease (PD). Ropinirole is rapidly absorbed after oral administration and undergoes extensive hepatic metabolism to active metabolites. The elimination half-life av. about six hours. Ropinirole has a low potential to interact with other drugs likely to be administered to PD patients. In patients with early PD, initial monotherapy with ropinirole was more effective than placebo or bromocriptine in the absence of selegiline and was as effective as bromocriptine in the presence of selegiline. Ropinirole was as effective as levodopa in patients with earlier stages of PD. In one subset of patients with advanced PD not adequately controlled by levodopa, adjunctive ropinirole was more effective than placebo and bromocriptine. Ropinirole was more effective than bromocriptine in patients previously given high-dose levodopa and was as effective in patients previously given low-dose levodopa or adjunctive dopamine agonist therapy. The most frequent adverse effects are nausea, somnolence, and dizziness; the dosage should be increased gradually to minimize adverse effects. Ropinirole is less expensive than bromocriptine and pergolide and similar in cost to pramipexole. Ropinirole appears to be a useful addition to existing therapeutic approaches to PD and is approved for both early and later stages of the disease.

OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 15 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1997:422228 CAPLUS
DOCUMENT NUMBER: 127:103729
ORIGINAL REFERENCE NO.: 127:19807a,19810a
TITLE: Pharmacologic options for managing Parkinson's disease
AUTHOR(S): Evidente, Virgilio G. H.; Adler, Charles H.
CORPORATE SOURCE: Mayo Clinic, Scottsdale, AZ, USA
SOURCE: Formulary (1997), 32(6), 594-596, 601-602, 604, 607-610
CODEN: FORMF9; ISSN: 1082-801X

PUBLISHER: Advanstar
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 54 refs. Current therapy for idiopathic Parkinson's disease (IPD) is mainly symptomatic with the focus on individualizing therapy for early and advanced stage disease. The most effective drug for both early and advanced IPD is levodopa. For patients with mild disease and minimal disability, monotherapy with anticholinergic agents, amantadine, selegiline, or dopamine agonists (eg, bromocriptine and pergolide) may be useful. Advanced disease is usually associated with levodopa-induced complications, such as motor fluctuations and dyskinesias, which may be alleviated by adjusting levodopa dosing or by adding a dopamine agonist. Although no drug has been unequivocally proven to be neuroprotective in IPD, selegiline, amantadine, bromocriptine, and pergolide may play some role in delaying the progression of disease.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 16 OF 48 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2002328044 EMBASE

TITLE: [The evolution of use of anti-Parkinson drugs in Spain].
Evolucion del consumo de farmacos antiparkinsonianos en Espana.

AUTHOR: Montane, E.; Vallano, A., Dr. (correspondence); Castel, J.M.

CORPORATE SOURCE: Servicio de Farmacologia Clinica, Hospital Universitario Vall d'Hebron, Passeig de la Vall d'Hebron, 119-129 E-08035 Barcelona, Spain. tv@icf.uab.es

SOURCE: Revista de Neurologia, (1 Apr 2002) Vol. 34, No. 7, pp. 612-617.
Refs: 43

ISSN: 0210-0010 CODEN: RVNRAA

COUNTRY: Spain

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 036 Health Policy, Economics and Management
037 Drug Literature Index
008 Neurology and Neurosurgery

LANGUAGE: Spanish; Castilian

SUMMARY LANGUAGE: English; Spanish; Castilian; Portuguese

ENTRY DATE: Entered STN: 3 Oct 2002

Last Updated on STN: 3 Oct 2002

AB Introduction. In recent years new anti-Parkinson drugs have been marketed and there has been controversy over the safety of some drugs. Objective. To analyze the evolution of the consumption of anti-Parkinson drugs and the effect of the newer drugs. Patients and methods. A study of the consumption of anti-Parkinson drugs (1989-1998). Data were obtained from the ECOM database of the Ministry of Health and TEMPUS of the National Statistics Institute. The drugs were classified using the Anatomico-Therapeutic-Clinical Classification (ATC). Consumption was expressed in defined daily dosage (DDD) and the costs in euros (€). The drugs marketed since 1990 were classified as new drugs and the others as classical drugs. Results. The total consumption of drugs increased from 1.92 DDD/1,000 inhabitants/day in 1989 to 3.64 DDD/1,000 inhabitants/day in 1998. The drugs showing the greatest increase were selegiline, pergolide and levodopa. The total pharmaceutical expenses tripled. There was a smaller increase in the consumption of new drugs (1.2% of the total in 1991 and 6.6% in 1998) than in their costs (6.7% of the total in 1991 and 38.8% in 1998). The

cost per DDD of the new drugs increased five times (1989: 2.55€ and 1998: 13.59€) and that of the classical drugs was similar (1989: 0.54€ and 1998: 0.62€). Conclusions. The total consumption of anti-Parkinson drugs has progressively increased. The consumption of selegiline has also increased in spite of controversy over its safety. The new drugs have a major economic effect.

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ACCESSION NUMBER: 2002036123 EMBASE
TITLE: [Switch from conventional selegiline to xilopar® allows dose reduction of levodopa and dopamine agonists].
Umstellung von konventionellen selegilin-präparaten auf xilopar® ermöglicht die reduktion von l-dopa und dopamin-agonisten.
AUTHOR: Holtmann, Wolfgang, Dr. (correspondence)
CORPORATE SOURCE: Arzt für Neurologie, Schlossplatz 6, 91207 Lauf, Germany.
SOURCE: Neurologie und Rehabilitation, (2001) Vol. 7, No. 6, pp. 298-300.
Refs: 4
ISSN: 0947-2177 CODEN: NEREF3
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: German
SUMMARY LANGUAGE: English; German
ENTRY DATE: Entered STN: 7 Feb 2002
Last Updated on STN: 7 Feb 2002

AB The anti-parkinsonian drug selegiline has successfully been used for years in order to achieve a levodopa sparing effect. The need for levodopa therapy can be delayed by an average of 9 months. In addition, various placebo-controlled studies demonstrated that the levodopa dose can be maintained almost stable for a period of at least 5 years when used in combination with selegiline. On the other hand, therapy with conventional selegiline is limited, e. g. by the contra-indication in patients with impaired hepatic or renal function, the possible disturbance of night-time sleep by the amphetamine metabolites, and by the high variability in bioavailability because of an extensive first-pass effect. In Xilopar®, selegiline is presented as a lyophilised tablet that can circumvent these problems. In this case report, the switch from conventional selegiline to Xilopar® lead to a dose reduction of levodopa as well as pergolide associated with very good symptom control. Xilopar® was well tolerated and resulted in a considerable improvement of the patient's quality of life.

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ACCESSION NUMBER: 2001212834 EMBASE
TITLE: [Pharmacotherapy of idiopathic parkinson's syndrome with special focus on neuroprotection].
Pharmakotherapie des idiopathischen parkinson-syndroms unter besonderer berücksichtigung neuroprotektiver therapiestrategien.
AUTHOR: Reichmann, H., Dr. (correspondence); Sommer, U.; Gerlach, M.; Riederer, P.
CORPORATE SOURCE: Klinik und Poliklinik für Neurologie, Univ. klinikum Carl Gustav Carus, Technische Universität Dresden, Fetscherstrasse 74, D-01307 Dresden, Germany.
SOURCE: Nervenheilkunde, (2001) Vol. 20, No. 4, pp. 227-236.

Refs: 44
 ISSN: 0722-1541 CODEN: NERVDI
 COUNTRY: Germany
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 037 Drug Literature Index
 008 Neurology and Neurosurgery
 LANGUAGE: German
 SUMMARY LANGUAGE: English; German
 ENTRY DATE: Entered STN: 28 Jun 2001
 Last Updated on STN: 28 Jun 2001

AB Most of the commonly used antiparkinsonian drugs show neuroprotective potency when tested in tissue culture or animal models. Neuroprotection consists of measures which lead to prevention or delay of neuronal cell death. So far, there are no clinical studies which show undoubtably neuroprotection. Nonetheless, there are 3 PET- or SPECT-controlled studies with ropinirole, pergolide and promipexole finished which were designed to prove neuroprotection while taking dopamine agonists. This paper will further introduce studies with selegiline and NMDA receptor antagonists which indicate possible neuroprotection. Experimental data suggest studies with radical scavengers, coenzyme Q, iron chelators or antiapoptotic drugs such as flupirtine. Taking all consisting data into account we recommend to treat early Parkinsonism with a combination of selegiline, NMDA receptor antagonists and dopamine agonists.

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ACCESSION NUMBER: 2000395778 EMBASE
 TITLE: [Akathisia secondary to tolcapone. Report of a case].
 Acatisia secundaria a tolcapone. Reporte de un caso.
 AUTHOR: Colorado-Ochoa, H. (correspondence)
 CORPORATE SOURCE: Hospital ISSSTE, F. Magon 657-1 esq. de a llave, C.P. 91910
 Veracruz Ver, Mexico.
 SOURCE: Gaceta Medica de Mexico, (2000) Vol. 136, No. 5,
 pp. 505-509.
 Refs: 21
 ISSN: 0016-3813 CODEN: GMMEAK
 COUNTRY: Mexico
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 037 Drug Literature Index
 038 Adverse Reactions Titles
 008 Neurology and Neurosurgery
 LANGUAGE: Spanish; Castilian
 SUMMARY LANGUAGE: English; Spanish; Castilian
 ENTRY DATE: Entered STN: 13 Dec 2000
 Last Updated on STN: 13 Dec 2000

AB The purpose of this work is to report a case of tolcapone-induced akathisia. A 39-year-old woman with Parkinson's disease, Hohen-Yahr IV, Webster 18 points with 10 years within onset presented lack of clinical response to levodopa-carbidopa, pergolide, selegiline and trihexiphenidyl, showing freezing and wearing-off phenomena and choreic dyskinetic abnormal movements of the upper and lower extremities, during the six months previous to her evaluation. Her hepatic function was normal. Levodopa-carbidopa and selegiline were diminished to add tolcapone, as described elsewhere. During the first three weeks, the patient showed marked clinical improvement of previous complications and sustained improvement during 12.5 weeks. At the 13th week of tolcapone therapy the patient developed constant orofacial, trunk, and superior and lower limb involuntary movements associated to lack of stand still. Laboratory tests showed discrete elevation of oxaloacetic-glutamic transaminase, direct bilirubin, indirect bilirubin, and alkaline phosphatase. Electroencephalogram and

CT scan were normal. Tolcapone therapy was finished, and levodopacarbidopa, pergolide and selegiline were diminished, procuring the disappearance of akathisia within 72 h.

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ACCESSION NUMBER: 1999280119 EMBASE
TITLE: Long term role of pergolide as an adjunct therapy in Parkinson's disease: Influence on disability, blood pressure, weight and levodopa syndrome.
AUTHOR: Sharma, J.C. (correspondence); Ross, I.N.
CORPORATE SOURCE: Newark Hospital, Newark, Nottinghamshire NG24 4DE, United Kingdom. jsharma@lineone.net
SOURCE: Parkinsonism and Related Disorders, (Sep 1999) Vol. 5, No. 3, pp. 111-114.
Refs: 15
ISSN: 1353-8020 CODEN: PRDIFO
PUBLISHER IDENT.: S 1353-8020(99)00017-6
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
006 Internal Medicine
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 26 Aug 1999
Last Updated on STN: 26 Aug 1999

AB Pergolide is a dopamine agonist acting on D1 and D2 receptors and has been used as an adjunct therapy with levodopa. We have retrospectively investigated its role over a duration of upto six years in Parkinson's disease (PD) patients to study: (1) its influence on the progression of disability related to PD; (2) effect on blood pressure and weight during the treatment period; (3) whether the use of pergolide has a long term levodopa sparing effect; (4) and how is it tolerated during this period? We studied 43 patients who had been on adjunct therapy with pergolide in addition to levodopa for more than six months. Mean age was 66 years, mean duration of PD prior to adding pergolide was 8 years and final assessment was done after a mean duration of adjunct therapy of 29 (6-72) months. There was no progression of disease disability as assessed on Hoehn and Yahr stage ($p = 0.09$) and Webster score ($p = 0.20$), while there was an improvement in symptom score ($p = 0.001$). There was an insignificant reduction in the dose of levodopa at final assessment from 630 to 535 mg ($p = 0.06$). A significant number of patients were able to discontinue taking selegiline ($p = 0.002$). There was no change in the number of patients with hallucinations ($p = 0.15$) and dyskinesia ($p = 0.09$). There was a significant fall in weight ($p = 0.02$), systolic ($p = 0.023$) and diastolic blood pressure ($p = 0.03$). This fall did not correlate with age, dose of pergolide or levodopa or disease severity but was influenced by duration of treatment. Ten patients discontinued pergolide for minor reasons after a mean duration of therapy for 23 months. We conclude that pergolide is a valuable adjunct therapy with levodopa over a duration of upto six years to maintain control of motor symptoms of Parkinson's disease.

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ACCESSION NUMBER: 1997187973 EMBASE
TITLE: Pharmacologic options for managing Parkinson's disease.
AUTHOR: Evidente, Virgilio G. H.

CORPORATE SOURCE: Mayo Clinic, Scottsdale, AZ, United States.
 AUTHOR: Adler, Charles H., Dr. (correspondence)
 CORPORATE SOURCE: Parkinson's Dis. Movement Disord. C., Department of
 Neurology, Mayo Clinic, Scottsdale, AZ, United States.
 AUTHOR: Adler, Charles H., Dr. (correspondence)
 CORPORATE SOURCE: Department of Neurology, Mayo Clinic Scottsdale, 13400 Shea
 Blvd., Scottsdale, AZ 85259, United States.
 SOURCE: Formulary, (Jun 1997) Vol. 32, No. 6, pp.
 594-596+601-602+604+607-610.
 Refs: 54
 ISSN: 0098-6909 CODEN: FORMF9
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 037 Drug Literature Index
 008 Neurology and Neurosurgery
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 31 Jul 1997
 Last Updated on STN: 31 Jul 1997

AB Current therapy for idiopathic Parkinson's disease (IPD) is
 mainly symptomatic with the focus on individualizing therapy for early and
 advanced stage disease. The most effective drug for both early and
 advanced IPD is levodopa. For patients with mild disease and minimal
 disability, monotherapy with anticholinergic agents, amantadine,
 selegiline, or dopamine agonists (eg, bromocriptine and
 pergolide) may be useful. Advanced disease is usually associated
 with levodopa-induced complications, such as motor fluctuations and
 dyskinesias, which may be alleviated by adjusting levodopa dosing or by
 adding a dopamine agonist. Although no drug has been unequivocally proven
 to be neuroprotective in IPD, selegiline, amantadine,
 bromocriptine, and pergolide may play some role in delaying the
 progression of disease.

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ACCESSION NUMBER: 1996251706 EMBASE
 TITLE: Controversies in the treatment of Parkinson's disease.
 AUTHOR: Hely, Mariese A.; Morris, John G.L. (correspondence)
 CORPORATE SOURCE: Department of Neurology, Westmead Hospital, Sydney, NSW
 2145, Australia.
 SOURCE: Current Opinion in Neurology, (1996) Vol. 9, No.
 4, pp. 308-313.
 Refs: 43
 ISSN: 1350-7540 CODEN: CONEEX
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 037 Drug Literature Index
 038 Adverse Reactions Titles
 008 Neurology and Neurosurgery
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 17 Sep 1996
 Last Updated on STN: 17 Sep 1996

AB Although theoretical reasons exist for believing that selegiline
 slows the progression of Parkinson's disease, this has not been
 shown in clinical trials. Selegiline improves the symptoms of
 Parkinson's disease, allowing the introduction of levodopa to be
 delayed in de-novo patients and, later, for levodopa to be used at a lower
 dose. It does not lessen the long-term problems of dyskinesia and
 fluctuations associated with levodopa therapy. The report of an increased
 mortality associated with selegiline therapy awaits further
 evaluation. Of the dopamine agonists, pergolide appears to be

more potent than bromocriptine; cabergoline looks promising. The catechol-O-methyltransferase inhibitors, tolcapone and entacapone, prolong the duration of action of levodopa and also show promise. The main objective in the drug treatment of Parkinson's disease remains the optimization of the dose and frequency of levodopa administration.

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ACCESSION NUMBER: 1995243051 EMBASE

TITLE: The therapeutic potential of moclobemide, a reversible selective monoamine oxidase A inhibitor in Parkinson's disease.

AUTHOR: Sieradzan, K., Dr. (correspondence); Channon, S.; Ramponi, C.; Stern, G.M.; Lees, A.J.; Youdim, M.B.H.

CORPORATE SOURCE: Department of Neurology, Manchester Royal Infirmary, Oxford Road, Manchester M13, United Kingdom.

SOURCE: Journal of Clinical Psychopharmacology, (1995)
Vol. 15, No. 4 SUPPL. 2, pp. 51S-59S.
ISSN: 0271-0749 CODEN: JCPYDR

COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article; (Conference paper)

FILE SEGMENT: 020 Gerontology and Geriatrics
030 Clinical and Experimental Pharmacology
032 Psychiatry
037 Drug Literature Index
008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 6 Sep 1995

Last Updated on STN: 6 Sep 1995

AB Dopamine is equally well deaminated oxidatively by monoamine oxidase (MAO) A and B types. Selegiline (L-deprenyl), a selective inhibitor of MAO-B, ameliorates the 'wearing off' akinesia and delays the need for levodopa in mild, previously untreated Parkinson's disease. The therapeutic potential of selective inhibition of MAO-A in Parkinson's disease has not been examined in detail. MAO-A accounts for only about 20% of total MAO activity in the human basal ganglia, and it differs from MAO-B in distribution. In contrast to MAO-B, which is confined to the extraneuronal compartment, MAO-A is found both extraneuronally and within the presynaptic dopaminergic terminals. The inhibition of MAO-A might alter the intraneuronal handling of dopamine reuptaken from synaptic clefts and thereby prolong oral levodopa benefit. We have given moclobemide, a selective, reversible inhibitor of MAO-A, to nondepressed patients with Parkinson's disease receiving standard levodopa/peripheral decarboxylase inhibitor or levodopa with dopaminergic agonist (bromocriptine, pergolide). Selegiline was discontinued at least 8 weeks earlier. A standard oral levodopa challenge was performed at the patient's entry to the study and repeated on the 22nd day of moclobemide treatment (150 mg thrice daily). The overall timespent 'on' and 'off' before the onset of treatment and during the last week on the drug was estimated from the patients' diaries. Neuropsychological assessments were also made before and after 3 weeks of moclobemide to measure possible effects on cognitive performance and mood. In acute levodopa challenge, the latency of motor response was significantly shortened and its duration was prolonged during moclobemide treatment. Similarly, the Webster's scores in 'off' state after overnight withdrawal of dopaminergic medication improved on moclobemide. In nondepressed parkinsonian patients, moclobemide did not alter mood and cognitive measures. The mild symptomatic effect and good tolerance with standard therapy suggest that moclobemide may be a particularly useful antidepressant in Parkinson's disease.

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ACCESSION NUMBER: 1994376272 EMBASE
TITLE: Early idiopathic parkinsonism: Initiation and optimization of treatment.
AUTHOR: Calne, D.B., Dr. (correspondence)
CORPORATE SOURCE: Neurodegenerative Disorders Centre, Faculty of Medicine, Vancouver Hospital, Vancouver, BC V6T 2B5, Canada.
SOURCE: Clinical Neuropharmacology, (1994) Vol. 17, No. SUPPL. 2, pp. S14-S18.
ISSN: 0362-5664 CODEN: CLNEDB
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 18 Jan 1995
Last Updated on STN: 18 Jan 1995

AB Once a diagnosis of idiopathic parkinsonism has been made, the choice and timing of therapy depend almost entirely on the patient's need for symptomatic relief, as no presently available therapy has any effect on the pathogenesis of the disease. Five categories of drugs are available for the treatment of idiopathic parkinsonism. Anticholinergic agents are effective against tremor but have prominent adverse effects. Amantadine has similar effects but is more active against rigidity and bradykinesia. Selegiline is a monoamine oxidase-B inhibitor; once thought to affect the pathogenesis of idiopathic parkinsonism, it is now known to offer only symptomatic relief. The dopamine agonists (bromocriptine, pergolide, and lisuride) stimulate D(2) receptors; they have antiparkinsonian effects and tolerance profiles broadly similar to those of levodopa but are slightly less efficacious. Pleural effusions and pulmonary fibrosis are unusual but important complications of these drugs; chest x-ray examinations are therefore recommended for all patients starting such treatment. Levodopa (combined with an extracerebral decarboxylase inhibitor to prevent nausea, the main adverse effect) has become the standard antiparkinsonism treatment. Patients using this preparation can suffer considerable variations in mobility and dyskinesia, which may be related to rapid, large-scale oscillations in plasma levodopa concentrations. Controlled-release (CR) preparations have been developed in an attempt to minimize these fluctuations and reduce long-term side effects. There is no universally agreed treatment for idiopathic parkinsonism. However, experience shows that a good balance of antiparkinsonian activity and adverse effects can be obtained by initiating treatment with a combination of levodopa and a decarboxylase inhibitor. A dopamine agonist can be added if the disease progresses and increased therapeutic activity is required.

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ACCESSION NUMBER: 1994119237 EMBASE
TITLE: Treatment of Parkinson's disease: From theory to practice.
AUTHOR: Ahlskog, J.E., Dr. (correspondence)
CORPORATE SOURCE: Department of Neurology, Mayo Clinic, Rochester, MN 55905, United States.
SOURCE: Postgraduate Medicine, (1994) Vol. 95, No. 5, pp. 52-54+57-58+61-64+68-69.
ISSN: 0032-5481 CODEN: POMDAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)

FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 May 1994
Last Updated on STN: 11 May 1994

AB Parkinson's disease responds rather dramatically to levodopa therapy during the first several years of treatment. With advancing disease, however, symptom control becomes more erratic, and some symptoms may become refractory to treatment. The use of selegiline hydrochloride (Eldepryl) has been proposed to slow the progression of Parkinson's disease; however, current evidence suggests that it is only partially effective at best, and there is no definite proof of a neuroprotective effect. Nonetheless, it is a reasonable treatment choice. Carbidopa-levodopa (Sinemet) remains the foundation of symptomatic treatment of Parkinson's disease. Clinical fluctuations occurring with advancing disease may be at least partially controlled by appropriate adjustments in dosage. A direct-acting dopamine agonist, bromocriptine mesylate (Parlodel) or pergolide mesylate (Permax), can be very helpful as adjunctive therapy to smooth these clinical fluctuations. Excessive intracellular oxidative stress has been proposed as a cause of Parkinson's disease; however, a recent multicenter trial investigating the use of high doses of the antioxidant vitamin E showed it to be ineffective. Whether other forms of nonspecific antioxidant therapy will prove beneficial is open to speculation.

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ACCESSION NUMBER: 1993251624 EMBASE
TITLE: Strategies in the treatment of early Parkinson's disease.
AUTHOR: Rinne, U.K. (correspondence)
CORPORATE SOURCE: Department of Neurology, University of Turku, SF-20520 Turku, Finland.
SOURCE: Acta Neurologica Scandinavica, Supplement, (1993)
Vol. 87, No. 146, pp. 50-53.
ISSN: 0065-1427 CODEN: ANSLAC
COUNTRY: Denmark
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 26 Sep 1993
Last Updated on STN: 26 Sep 1993

AB Over recent years I have been studying whether dopamine agonist treatment alone, or in early combination with levodopa, might institute a better long-term treatment in Parkinson's disease than levodopa alone. Indeed, early combination of levodopa with bromocriptine, pergolide or lisuride has indicated that this kind of treatment results in better management of Parkinson's disease with fewer fluctuations in disability, especially end-of-dose disturbances and dyskinesias, than treatment with levodopa alone. Furthermore, similar results were obtained by using lisuride in combination with selegiline and levodopa. Thus, it appears advisable to initiate the dopaminergic treatment in early Parkinson's disease by using a combination of selegiline, levodopa and a dopamine agonist. There are many ways of building up this kind of treatment. Instead of levodopa, it is possible to use initially a dopamine agonist and to add selegiline and levodopa when the therapeutic response becomes insufficient. Another alternative would be to start with selegiline alone, then to add a dopamine agonist and, finally, levodopa when clinically indicated.

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ACCESSION NUMBER: 1992116942 EMBASE
TITLE: Parkinson's disease: Update on pharmacologic options to slow progression and treat symptoms.
AUTHOR: Ahlskog, J.E.
SOURCE: Hospital Formulary, (1992) Vol. 27, No. 2, pp. 146-163.
ISSN: 0098-6909 CODEN: HOFOD9
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 15 May 1992
Last Updated on STN: 15 May 1992

AB Medical treatment of Parkinson's disease is becoming increasingly complex. Carbidopa/levodopa continues to be the most efficacious medication available. Other recent evidence suggests that selegiline might slow Parkinson's disease progression. The direct-acting dopamine agonists, bromocriptine and pergolide, are often beneficial in patients with short-duration, fluctuating levodopa responses. These medications have also been advocated for initial symptomatic treatment, concurrent with the initiation of carbidopa/levodopa; however, this use is controversial. The controlled-release formulation of carbidopa/levodopa typically prolongs the levodopa response by approximately 30%, but some patients prefer the standard formulation due to its faster onset of action. The expense of using two or more of these medications is of concern to this patient population.

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ACCESSION NUMBER: 1992035022 EMBASE
TITLE: New strategies in the treatment of early Parkinson's disease.
AUTHOR: Rinne, U.K. (correspondence)
CORPORATE SOURCE: Department of Neurology, University of Turku, SF-20520 Turku, Finland.
SOURCE: Acta Neurologica Scandinavica, Supplement, (1991) Vol. 84, No. 136, pp. 95-98.
ISSN: 0065-1427 CODEN: ANSLAC
COUNTRY: Denmark
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Mar 1992
Last Updated on STN: 20 Mar 1992

AB Over recent years I have been studying whether dopamine agonist treatment alone, or in early combination with levodopa, might institute a better long-term treatment in Parkinson's disease than levodopa alone. Indeed, early combination of levodopa with bromocriptine, pergolide or lisuride has indicated that this kind of treatment results in better management of Parkinson's disease with fewer fluctuations in disability, especially end-of-dose disturbances and dyskinesias, than treatment with levodopa alone. Furthermore, similar results were obtained by using lisuride in combination with selegiline and levodopa. However, during long-term treatment the

changes in parkinsonian disability were equal in all treatment groups with or without selegiline. Thus, the possible efficacy of selegiline in slowing down the progression of Parkinson's disease requires further investigations. As a new treatment strategy it appears advisable to initiate the dopaminergic treatment in early Parkinson's disease by using initially selegiline and a dopamine agonist and by adding levodopa when the therapeutic response is insufficient. Another alternative would be to start with selegiline alone, then add a dopamine agonist and, finally, levodopa.

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ACCESSION NUMBER: 1991259533 EMBASE
TITLE: Behavioral complications of drug treatment of Parkinson's disease.
AUTHOR: Cummings, J.L.
CORPORATE SOURCE: Neurobehavior Unit, West LA VAMC, 11301 Wilshire Blvd., Los Angeles, CA 90073, United States.
AUTHOR: Cummings, J., Dr. (correspondence)
CORPORATE SOURCE: Neurobehavior Unit, West LA VAMC, 11301 Wilshire Blvd., Los Angeles, CA 90073, United States.
SOURCE: Journal of the American Geriatrics Society, (1991) Vol. 39, No. 7, pp. 708-716.
ISSN: 0002-8614 CODEN: JAGSAF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 020 Gerontology and Geriatrics
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Dec 1991
Last Updated on STN: 16 Dec 1991

AB A variety of neuropharmacologic agents, including anticholinergic drugs, amantadine hydrochloride, levodopa, selegiline, bromocriptine, and pergolide, are now available for the treatment of Parkinson's disease. Of patients treated with dopaminergic agents, 30% develop visual hallucinations, 10% exhibit delusions, 10% have euphoria, 1% have mania, 10% to 15% experience increased anxiety, 15% have confusional periods, and a few exhibit altered sexual behavior. Anticholinergic drugs have a greater tendency to produce confusional states than dopaminergic compounds. Elderly patients and those with underlying dementia are most likely to have untoward side effects with anti-parkinsonism treatment. Dosage reduction is the optimum management strategy, although anti-psychotic agents may be necessary in patients with delusions, and lithium may help control drug-induced mania. Dopaminergic agents share the property of stimulation of D2 dopamine receptors, and this action may play an essential role in mediating their neuropsychiatric effects.

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ACCESSION NUMBER: 1990048730 EMBASE
TITLE: New concepts in the treatment of Parkinson's disease.
AUTHOR: Ahlskog, J.E.; Wilkinson, J.M.
CORPORATE SOURCE: Mayo Medical School, Rochester, MN, United States.
SOURCE: American Family Physician, (1990) Vol. 41, No. 2, pp. 574-584.
ISSN: 0002-838X CODEN: AFPYAE

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 1991
Last Updated on STN: 13 Dec 1991

AB Carbidopa/levodopa remains the most potent drug for the treatment of Parkinson's disease. Several newer medications may help stabilize and improve such problems as fluctuating responses to the medication, drug-induced dyskinesias and refractory symptoms. Patients with fluctuating responses that do not respond to adjustments in the carbidopa/levodopa dose may benefit from the addition of a direct-acting dopamine agonist, such as pergolide or bromocriptine. While carbidopa/levodopa and the direct-acting dopamine agonists have a proven track record as symptomatic treatment, they probably do not alter the pathologic process underlying this progressive condition. On the other hand, two studies have shown that selegiline might slow the progression of Parkinson's disease, independent of any direct effects on symptoms.

L11 ANSWER 31 OF 48 Elsevier Biobase COPYRIGHT 2009 Elsevier Science B.V. on STN

ACCESSION NUMBER: 1998132047 ESBIODBASE
TITLE: Transcranial AC pulsed applications of weak electromagnetic fields reduces freezing and falling in progressive supranuclear palsy: A case report
AUTHOR(S): Sandyk, Reuven
CORPORATE SOURCE: Sandyk, Reuven (Department of Neuroscience, Inst. Biomed. Eng. and Rehab. Serv., Touro College, Dix Hills, NY 11746 (US))
SOURCE: International Journal of Neuroscience (May 1998) Volume 94, Number 1-2, pp. 41-54, 91 refs. CODEN: IJNUB7 ISSN: 0020-7454
COUNTRY OF PUBLICATION: United Kingdom
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jan 2009
Last updated on STN: 31 Jan 2009

AN 1998132047 ESBIODBASE

AB Freezing is a common and disabling symptom in patients with Parkinsonism. It affects most commonly the gait in the form of start hesitation and sudden immobility often resulting in falling. A high incidence of freezing occurs in patients with progressive supranuclear palsy (PSP) which is characterized clinically by a constellation of symptoms including supranuclear ophthalmoplegia, postural instability, axial rigidity, dysarthria, Parkinsonism, and pseudobulbar palsy. Pharmacologic therapy of PSP is currently disappointing and the disease progresses relentlessly to a fatal outcome within the first decade after onset. This report concerns a 67 year old woman with a diagnosis of PSP in whom freezing and frequent falling were the most disabling symptoms of the disease at the time of presentation. Both symptoms, which were rated 4 on the Unified Parkinson Rating Scale (UPRS) which grades Parkinsonian symptoms and signs from 0 to 4, with 0 being normal and 4 being severe symptoms, were resistant to treatment with dopaminergic drugs such as levodopa, amantadine, selegiline and pergolide mesylate as well as with the potent and highly selective noradrenergic reuptake inhibitor nortriptyline. Weekly transcranial applications of AC pulsed

electromagnetic fields (EMFs) of picotesla flux density was associated with approximately 50% reduction in the frequency of freezing and about 80-90% reduction in the frequency of falling after a 6 months follow-up period. At this point freezing was rated 2 while falling received a score of 1 on the UPRS. In addition, this treatment was associated with an improvement in Parkinsonian and pseudobulbar symptoms with the difference between the pre- and post EMF treatment across 13 measures being highly significant ($p < .005$; Sign test). These results suggest that transcranial administration AC pulsed EMFs in the picotesla flux density is efficacious in the treatment of PSP.

L11 ANSWER 32 OF 48 Elsevier Biobase COPYRIGHT 2009 Elsevier Science B.V. on STN

ACCESSION NUMBER: 1998069290 ES BIOBASE
TITLE: Speech impairment in Parkinson's disease is improved by transcranial application of electromagnetic fields
AUTHOR(S): Sandyk, Reuven
CORPORATE SOURCE: Sandyk, Reuven (Department of Neuroscience, Institute for Biomedical Engineering, Rehab. Services of Touro College, Dix Hills, NY 11746 (US))
SOURCE: International Journal of Neuroscience (Nov 1997) Volume 92, Number 1-2, pp. 63-72, 59 refs.
CODEN: IJNUB7 ISSN: 0020-7454
COUNTRY OF PUBLICATION: United Kingdom
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jan 2009
Last updated on STN: 31 Jan 2009

AN 1998069290 ES BIOBASE

AB A 52 year old fully medicated physician with juvenile onset Parkinsonism experienced 4 years ago severe 'on-off' fluctuations in motor disability and debilitating speech impairment with severe stuttering which occurred predominantly during 'on-off' periods. His speech impairment improved 20%-30% when sertraline (75 mg/day), a serotonin reuptake inhibitor, was added to his dopaminergic medications which included levodopa, amantadine, selegiline and pergolide mesylate. A more dramatic and consistent improvement in his speech occurred over the past 4 years during which time the patient received, on a fairly regular basis, weekly transcranial treatments with AC pulsed electromagnetic fields (EMFs) of picotesla flux density. Recurrence of speech impairment was observed on several occasions when regular treatments with EMFs were temporarily discontinued. These findings demonstrate that AC pulsed applications of picotesla flux density EMFs may offer a nonpharmacologic approach to the management of speech disturbances in Parkinsonism. Furthermore, this case implicates cerebral serotonergic deficiency in the pathogenesis of Parkinsonian speech impairment which affects more than 50% of patients. It is believed that pulsed applications of EMFs improved this patient's speech impairment through the facilitation of serotonergic transmission which may have occurred in part through a synergistic interaction with sertraline.

L11 ANSWER 33 OF 48 MEDLINE on STN

ACCESSION NUMBER: 2000512161 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11068454
TITLE: Wearing-off phenomenon--neurological approach.
AUTHOR: Ishikawa A
CORPORATE SOURCE: Department of Neurology, Nishi-Ojiya National Hospital.
SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2000 Oct) Vol. 58, No. 10, pp. 2100-3. Ref: 9
Journal code: 0420546. ISSN: 0047-1852.

PUB. COUNTRY: Japan
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 1 Feb 2001

AB The mechanism of the wearing-off phenomenon and the method of how to control it by means of anti-parkinsonian medications is described. To control the wearing-off phenomenon, it is useful to administer L-dopa before eating because absorption of L-dopa is less when competing with amino acids. Administration of L-dopa four or five times a day is also useful. Dopamin agonists(e.g., bromocriptine, pergolide, talipexole, and cabergoline), and monoamine oxidase inhibitors(e.g., selegiline) control the wearing-off phenomenon, and may also suppress its occurrence. As a specific method for controlling the wearing-off phenomenon, continuous administration of anti-parkinsonian drugs by the intra-alimentary tract or a subcutaneous injection is useful. It is important to avoid early wearing-off phenomenon when treating patients with Parkinson's disease.

L11 ANSWER 34 OF 48 MEDLINE on STN
ACCESSION NUMBER: 2000512155 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11068448
TITLE: The new Parkinson's disease drugs.
AUTHOR: Hasegawa K
CORPORATE SOURCE: Division of Neurology, Sagamihara National Hospital.
SOURCE: Nippon rinsho. Japanese journal of clinical medicine,
(2000 Oct) Vol. 58, No. 10, pp. 2066-71. Ref: 13
Journal code: 0420546. ISSN: 0047-1852.

PUB. COUNTRY: Japan
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 1 Feb 2001

AB The purpose of the new drugs for Parkinson's disease is control of the long-term levodopa treatment syndromes, especially wearing-off phenomenon and dyskinesia. Therefore, they show long T1/2. Most of them are classified into dopamine agonists. Others are monoamine oxidase B inhibitor and cathecole-o-methyltransferase inhibitor. Marketed dopamine agonists are bromocriptine, pergolide, talipexole, and cabergoline in Japan. Except talipexole, they are all ergot alkaloid derivatives. Their affinity for dopamine receptor is D2 group, and their T1/2 are longer than levodopa. Bromocriptine is an oldest dopamine agonist. Other 3 drugs and bromocriptine had made each other double blinded cross over trial previously. The result of double blinded studies show that their efficacy for PD treatment were equal, 40-50% patients with PD. However, in clinical usage, some difference is observed as described below. Efficacy of pergolide is strong compared with bromocriptine; however, pergolide is easy to arise dyskinesia. Talipexole is strong in the hypnosis effect. As for cabergoline, it takes long time to show medical effect, so that it is expected to control wearing-off phenomenon. Monoamine oxidase B inhibitor, Selegiline, is useful as an economizer effect to levodopa. As for the

cathechole-o-methyltransferase inhibitor (COMT-I) will be make double-blinded trial in future. The efficacy for PD treatment of COMT-I is prolonged levodopa effect for PD, so that wearing-off phenomenon will be controlled. To use these drugs successfully is important with the treatment of PD. In the future, the development of the cause therapy in addition to the systematic therapy is wanted.

L11 ANSWER 35 OF 48 MEDLINE on STN

ACCESSION NUMBER: 1996019379 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7487655
TITLE: Treatment of Parkinson's disease.
AUTHOR: Eadie M J
CORPORATE SOURCE: Department of Medicine, University of Queensland.
SOURCE: Australian family physician, (1995 Sep) Vol. 24,
No. 9, pp. 1685-7, 1690-2.
Journal code: 0326701. ISSN: 0300-8495.
PUB. COUNTRY: Australia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 24 Jan 1996
Last Updated on STN: 24 Jan 1996
Entered Medline: 13 Dec 1995

AB Early stage Parkinson's disease may be better left untreated if it does not limit motor function. Once limitation of function is present levodopa-dopa decarboxylase inhibitor combinations are the most effective therapy, although amantadine may be satisfactory for a time in milder cases. The optimal independent roles of the ergot derivatives bromocriptine and pergolide, and the MAOb inhibitor selegiline, are not yet generally agreed although they are accepted as useful in supplementing the effects of levodopa. With prolonged levodopa use various late-stage treatment problems may appear. The pathogenesis of these is poorly understood and no completely satisfactory ways of managing them are available.

L11 ANSWER 36 OF 48 MEDLINE on STN

ACCESSION NUMBER: 1995266329 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7747490
TITLE: Activation by selegiline (Eldepryle) of REM sleep behavior disorder in parkinsonism.
AUTHOR: Loudon M B; Morehead M A; Schmidt H S
CORPORATE SOURCE: West Virginia University School of Medicine, Morgantown, USA.
SOURCE: The West Virginia medical journal, (1995 Mar-Apr) Vol. 91, No. 3, pp. 101.
Journal code: 0413777. ISSN: 0043-3284.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 21 Jun 1995
Last Updated on STN: 21 Jun 1995
Entered Medline: 9 Jun 1995

AB Abnormal sleep-wake organization is frequently seen in idiopathic parkinsonism (PD) and other parkinsonism syndromes. A 1993 article in The Annals of Neurology first described the high rate of REM behavior disorder (RBD) in non-demented PD patients (1). In this article, we present the case reports of three non-demented PD patients who manifested RBD while on recommended doses of selegiline

(Eldepryle). None of them had problems severe enough to suggest RBD while they were being treated with varying doses of other dopaminergic agents (carbidopa/L-dopa, pergolide) unaccompanied by selegiline.

L11 ANSWER 37 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1994323057 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7914010
TITLE: Initiating treatment for idiopathic parkinsonism.
AUTHOR: Calne D B
CORPORATE SOURCE: Department of Medicine, University of British Columbia, Vancouver, Canada.
SOURCE: Neurology, (1994 Jul) Vol. 44, No. 7 Suppl 6, pp. S19-22. Ref: 10
Journal code: 0401060. ISSN: 0028-3878.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 9 Sep 1994
Last Updated on STN: 6 Feb 1995
Entered Medline: 26 Aug 1994

AB The initial decision in the management of idiopathic parkinsonism is whether any pharmacotherapy is indicated. There is no conclusive evidence that treatment is helpful before symptoms start to affect the patient's life, although some neurologists believe that deprenyl, also known as selegiline, could be useful. Once functional deficits begin to interfere with the patient's work or social activities, treating symptoms becomes appropriate. Anticholinergics and amantadine can be used, but their limited benefit is often accompanied by unacceptable adverse effects. Dopaminomimetics are the most satisfactory medications, including levodopa and such artificial dopamine agonists as bromocriptine, pergolide, or lisuride.

L11 ANSWER 38 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1994203934 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8153048
TITLE: Treatment of Parkinson's disease. From theory to practice.
AUTHOR: Ahlskog J E
CORPORATE SOURCE: Department of Neurology, Mayo Clinic, Rochester, MN 55905.
SOURCE: Postgraduate medicine, (1994 Apr) Vol. 95, No. 5, pp. 52-4, 57-8, 61-4 passim. Ref: 25
Journal code: 0401147. ISSN: 0032-5481.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 23 May 1994
Last Updated on STN: 23 May 1994
Entered Medline: 10 May 1994

AB Parkinson's disease responds rather dramatically to levodopa therapy during the first several years of treatment. With advancing disease, however, symptom control becomes more erratic, and some symptoms may become refractory to treatment. The use of selegiline hydrochloride (Eldepryl) has been proposed to slow the progression of Parkinson's disease; however, current evidence suggests that it is only partially effective at best, and there is no definite proof of a

neuroprotective effect. Nonetheless, it is a reasonable treatment choice. Carbidopa-levodopa (Sinemet) remains the foundation of symptomatic treatment of Parkinson's disease. Clinical fluctuations occurring with advancing disease may be at least partially controlled by appropriate adjustments in dosage. A direct-acting dopamine agonist, bromocriptine mesylate (Parlodel) or pergolide mesylate (Permax), can be very helpful as adjunctive therapy to smooth these clinical fluctuations. Excessive intracellular oxidative stress has been proposed as a cause of Parkinson's disease; however, a recent multicenter trial investigating the use of high doses of the antioxidant vitamin E showed it to be ineffective. Whether other forms of nonspecific antioxidant therapy will prove beneficial is open to speculation.

L11 ANSWER 39 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1992261536 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1350053
TITLE: An integrated approach to patient management in Parkinson's disease.
AUTHOR: Lieberman A
CORPORATE SOURCE: Movement Disorders Department, Barrow Neurological Institute, St. Josephs Medical Center, Phoenix, Arizona.
SOURCE: Neurologic clinics, (1992 May) Vol. 10, No. 2, pp. 553-65. Ref: 35
Journal code: 8219232. ISSN: 0733-8619.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 26 Jun 1992
Last Updated on STN: 6 Feb 1995
Entered Medline: 17 Jun 1992

AB New concepts about the pathogenesis and pathophysiology of Parkinson's disease have emerged. For these concepts to be useful, they must be understood, and for them to be applied, the psychology of the patient and the patient's family must be understood. The initial consultation is crucial in establishing a successful relationship between a patient, family, and physician. This consultation is analyzed and ways of avoiding errors and misconceptions delineated. Emphasis is placed on imaginative questioning using the format of the ADL portion of the UPDRS in establishing the diagnosis and following treatment. The rationale for starting treatment with selegiline at this time is discussed in the context of the role that increased MAO-B activity plays in the progression of Parkinson's disease. After making the diagnosis and starting treatment with selegiline, deciding when to start levodopa is the next crucial decision. Often as important as deciding when to start levodopa is overcoming the resistance of the patient to accept this treatment. The next crucial decision occurs after the patient develops response fluctuations on levodopa. A format for assessing the fluctuations is presented, and the merits of different treatments, including selegiline, dopamine agonists (bromocriptine and pergolide), and sustained-release or controlled-release levodopa preparations (Sinemet CR), discussed. The management of patients with depression, sleep problems, and advanced disease including postural instability and mental changes are reviewed.

L11 ANSWER 40 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1992195439 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1347909
TITLE: Initiating treatment of Parkinson's disease.
AUTHOR: Koller W C

CORPORATE SOURCE: Department of Neurology, University of Kansas Medical Center, Kansas City, KS 66103.
SOURCE: Neurology, (1992 Jan) Vol. 42, No. 1 Suppl 1, pp. 33-8; discussion 57-60. Ref: 67
Journal code: 0401060. ISSN: 0028-3878.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 9 May 1992
Last Updated on STN: 6 Feb 1995
Entered Medline: 20 Apr 1992

AB Treatment of Parkinson's disease (PD) can be divided into two categories: symptomatic therapy (restoring dopamine levels toward normal and reversing functional disability) and preventive therapy (interfering with the pathophysiologic mechanism of PD to prevent or decrease the rate of progression of the disease). Regarding symptomatic treatment, although anticholinergic preparations generally are considered effective for the symptoms of tremor and rigidity without altering bradykinesia, their effectiveness is limited and adverse reactions are common; their role should be restricted to use as adjuvants to levodopa therapy. Amantadine has been shown to be as effective as anticholinergics, but it lacks long-term efficacy. Dopamine agonists--bromocriptine, pergolide mesylate and lisuride in Europe--are not as effective as levodopa and therefore rarely are used as initial therapy; their proposed role, too, is as adjuvants to levodopa therapy. Levodopa is the most effective drug presently available for the treatment of PD; its introduction is accompanied by rapid and dramatic reduction of symptoms and signs. Initial adverse reactions are not usually a major problem; and although there is speculation that initiation of therapy should be delayed because of possible long-term complications, clinically distinguishing these from problems related to disease progression itself is difficult. The possibility that nigral cell death is mediated by oxidative mechanisms provides the basis for considering antioxidant therapy as protective treatment; selegiline, an antioxidant, has been found to delay the need for symptomatic therapy. It is suggested that initial treatment of Parkinson's disease begin with both preventive therapy with selegiline and symptomatic treatment with the sustained-release preparation of levodopa, which may be associated with fewer long-term complications.

L11 ANSWER 41 OF 48 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 1995:274401 SCISEARCH
THE GENUINE ARTICLE: QT862
TITLE: THE RATIONALE FOR THE USE OF DOPAMINE AGONISTS IN PARKINSONS-DISEASE
AUTHOR: JENNER P (Reprint)
CORPORATE SOURCE: UNIV LONDON KINGS COLL, NEURODEGENERAT DIS RES CTR, DIV BIOMED SCI, PHARMACOL GRP, MANRESA RD, LONDON SW3 6LX, ENGLAND (Reprint)
COUNTRY OF AUTHOR: ENGLAND
SOURCE: NEUROLOGY, (MAR 1995) Vol. 45, No. 3, Supp. [3], pp. 6-12.
ISSN: 0028-3878.
PUBLISHER: LITTLE BROWN CO, 34 BEACON STREET, BOSTON, MA 02108-1493.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 51

ENTRY DATE: Entered STN: 1995
Last Updated on STN: 1995

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Experimental and clinical studies indicate that both dopamine D-2-like and D-1-like receptors are important in reversing the motor symptoms of Parkinson's disease, and therefore stimulation of both D-1 and D-2 receptors may be advantageous in its treatment. At present, the role of other receptor subtypes, such as the D-3 receptor, remains unknown, although in primates the D-3 receptor might be of importance because it exists in significant amounts within the caudate-putamen. Both D-1 and D-2 agonists induce dyskinesias in drug-naive, MPTP-treated primates and provoke dyskinesias in levodopa-primed animals. D-1 agonists in low doses, however, might have antiparkinsonian effects without inducing dyskinesias, and on repeated administration perhaps can diminish the intensity of dyskinesias in levodopa-primed, MPTP-treated primates. The production of dyskinesias in Parkinson's disease might reflect an imbalance in the D-1-direct and D-2-indirect GABAergic output pathways from the caudate-putamen, which colocalize tachykinins and enkephalins, respectively. Destruction of the nigrostriatal pathway decreases the mRNA for substance P but elevates the mRNA for enkephalin. Treatment with levodopa reverses the decrease in substance P mRNA but has either a partial or no effect on mRNA for enkephalin. This suggests that levodopa treatment leads to a new imbalance between output from the striatum through the direct and indirect pathways. In contrast, dopamine agonists appear less able than levodopa to manipulate basal ganglia outflow. This might reflect their decreased ability to reverse parkinsonian motor deficits or the greater ability of levodopa to provoke dyskinesias. Dopamine agonist drugs also might exert neuroprotective actions. Pergolide, like selegiline, elevates superoxide dismutase activity in brain, decreases hydrogen peroxide formation from dopamine, and preserves nigral cells in aging rats. Bromocriptine, apomorphine, and other agonists also scavenge free radicals and show antioxidant activity, compared with the mainly pro-oxidant actions of levodopa.

L11 ANSWER 42 OF 48 TOXCENTER COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1997:836 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 34-11266
TITLE: Drug treatment of Parkinson's disease in the 1990s: achievements and future possibilities
AUTHOR(S): Hughes, A. J.
CORPORATE SOURCE: Neurol. Dept., Austin and Repatriation Med. Ctr., Repatriation Campus, Banksia St., West Heidelberg, VIC 3081, Australia
SOURCE: Drugs (New Zealand), (Feb 1997) Vol. 53, pp. 195-205. 65 Refs.
CODEN: DRUGAY. ISSN: 0012-6667.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 97:3096
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB Advances in the medical treatment of Parkinson disease, current therapies with levodopa, bromocriptine, pergolide, selegiline, amantadine, and anticholinergic agents, and the management of drug induced dyskinesias are discussed.
Rosemary Gregor

L11 ANSWER 43 OF 48 TOXCENTER COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1993:51662 TOXCENTER
DOCUMENT NUMBER: PubMed ID: 8101417
TITLE: Strategies in the treatment of early Parkinson's disease
AUTHOR(S): Rinne U K
CORPORATE SOURCE: Department of Neurology, University of Turku Finland
SOURCE: Acta neurologica Scandinavica. Supplementum, (1993
) Vol. 146, pp. 50-3. Ref: 26.
Journal code: 0370337. ISSN: 0065-1427.
COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
FILE SEGMENT: MEDLINE
OTHER SOURCE: MEDLINE 1993325359
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 31 Jul 2007

AB Over recent years I have been studying whether dopamine agonist treatment alone, or in early combination with levodopa, might institute a better long-term treatment in Parkinson's disease than levodopa alone. Indeed, early combination of levodopa with bromocriptine, pergolide or lisuride has indicated that this kind of treatment results in better management of Parkinson's disease with fewer fluctuations in disability, especially end-of-dose disturbances and dyskinesias, than treatment with levodopa alone. Furthermore, similar results were obtained by using lisuride in combination with selegiline and levodopa. Thus, it appears advisable to initiate the dopaminergic treatment in early Parkinson's disease by using a combination of selegiline, levodopa and a dopamine agonist. There are many ways of building up this kind of treatment. Instead of levodopa, it is possible to use initially a dopamine agonist and to add selegiline and levodopa when the therapeutic response becomes insufficient. Another alternative would be to start with selegiline alone, then to add a dopamine agonist and, finally, levodopa when clinically indicated.

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ACCESSION NUMBER: 1992:83 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 29-04761
TITLE: Parkinson's disease: update on pharmacologic options to slow progression and treat symptoms
AUTHOR(S): Ahlskog, J. E.
CORPORATE SOURCE: Mayo Clin., Dept. of Neurol., 200 First St. SW, Rochester, MN 55905, USA
SOURCE: Hospital Formulary (USA), (Feb 1992) Vol. 27, pp. 146-152, 161-163. 92 Refs.
CODEN: HOFOD9. ISSN: 0098-6909.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 92:231
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB Parkinson's disease, including therapy for early and late disease, results of clinical studies, drug interactions, adverse effects, and costs of medications, is discussed. Drug therapy with such agents as selegiline, alpha-tocopherol, levodopa, bromocriptine, pergolide, carbidopa/levodopa (Sinemet CR), and adjunctive therapy with baclofen (Lioresal) and antidepressants are included.
Kate Gibbons

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ACCESSION NUMBER: 1991:2681 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 29-08653
TITLE: Drug therapy for Parkinson's disease
AUTHOR(S): Shimp, L. A.
SOURCE: Journal Michigan Pharmacist, (Dec 1991) Vol. 29,
pp. 448-451, 453.
ISSN: 0026-2404.

DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 91:11025
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB The pathologic brain changes that cause the signs and symptoms of Parkinson's disease and the use and side effects of anticholinergics, levodopa-carbidopa, amantadine, bromocriptine, pergolide, and selegiline are discussed. This article qualifies for one hour of U.S. CE credit by the ACPE.
Anne L. Morisseau

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ACCESSION NUMBER: 1990:481 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 27-12453
TITLE: New alternatives for the treatment of Parkinson's disease
AUTHOR(S): Erwin, W. G.
CORPORATE SOURCE: Philadelphia Coll. of Pharm. and Sci., Philadelphia, PA,
USA
SOURCE: American Druggist (USA), (Feb 1990) Vol. 201,
pp. 62, 64, 66, 68, 70, 72.
CODEN: AMDRAG. ISSN: 0190-5279.

DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 90:1519
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB The pathophysiology, clinical symptoms and treatment of Parkinson disease are discussed. Long term complications of levodopa therapy and the use, dosage and problems associated with pergolide mesylate (Permax) and selegiline hydrochloride (Eldepryl) are described. This article qualifies for 2 hours U.S. CE credit by the ACPE.
Ellen Katz Neumann

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ACCESSION NUMBER: 1989:1668 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 27-03204
TITLE: Pergolide and selegiline for Parkinson's disease
AUTHOR(S): anon
SOURCE: Medical Letter on Drugs and Therapeutics (USA), (Sep 8 1989) Vol. 31, pp. 81-83. 16 Refs.
CODEN: MELEAP. ISSN: 0025-732X.

DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 89:5438
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB The pharmacology, pharmacokinetics, clinical effectiveness, adverse effects and dosage of 2 newly approved antiparkinson agents,

pergolide mesylate (Permax) and selegiline hydrochloride (Eldepryl) are reported.
Victor Origoni

L11 ANSWER 48 OF 48 TOXCENTER COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1988:2925 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 26-11477
TITLE: Drugs for parkinsonism
AUTHOR(S): anon
SOURCE: Medical Letter on Drugs and Therapeutics (USA), (Dec 16 1988) Vol. 30, pp. 113-116.
CODEN: MELEAP. ISSN: 0025-732X.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 88:10326
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB The mechanism of action, clinical effects, limitations, and adverse effects of drugs used in the treatment of Parkinson disease are presented. Drugs covered include levodopa alone and in combination with carbidopa (Sinemet), bromocriptine mesylate (Parlodel), anticholinergic agents, amantadine hydrochloride (Symmetrel), selegiline hydrochloride (Eldepryl), pergolide (Permax), lisuride, controlled release Sinemet, and adjunctive antidepressants.
Lisa Webster

=> END

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FULL ESTIMATED COST	284.11	307.67
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CA SUBSCRIBER PRICE	-6.56	-6.56

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L9 ANSWER 310 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 236

ACCESSION NUMBER: 1983118184 EMBASE
TITLE: Controlled trial of pergolide mesylate in Parkinson's disease and progressive supranuclear palsy.
AUTHOR: Jankovic, J.
CORPORATE SOURCE: Dep. Neurol., Baylor Coll. Med., Texas Med. Cent., Houston, TX 77030, United States.
SOURCE: Neurology, (1983) Vol. 33, No. 4, pp. 505-507.
ISSN: 0028-3878 CODEN: NEURAI
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Dec 1991
Last Updated on STN: 9 Dec 1991

AB We evaluated pergolide in 22 patients with Parkinson's disease and 3 with progressive supranuclear palsy (PSP). After achieving an optimal dose of pergolide and Sinemet, a matching placebo was substituted in double-blind manner. The mean dose of levodopa (in Sinemet) was reduced by 68%; in eight patients, pergolide completely replaced levodopa. In parkinsonian patients, the mean Hoehn-Yahr stage decreased from 3.2 to 1.6, and the mean total disability score decreased from 48.3 to 17.8. In 10 patients with on-off phenomenon, the time on increased 174% with pergolide. There was little effect in PSP. Postural light-headedness and reversible mental changes were seen.

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ACCESSION NUMBER: 1983:278112 BIOSIS
DOCUMENT NUMBER: PREV198376035604; BA76:35604
TITLE: PROGRESSIVE SUPRANUCLEAR PALSY CLINICAL FEATURES AND RESPONSE TO TREATMENT IN 16 PATIENTS.
AUTHOR(S): JACKSON J A [Reprint author]; JANKOVIC J; FORD J
CORPORATE SOURCE: DEP NEUROLOGY, BAYLOR MED, TEX MED CENTER, HOUSTON, TEX 77030, USA
SOURCE: Annals of Neurology, (1983) Vol. 13, No. 3, pp. 273-278.
CODEN: ANNED3. ISSN: 0364-5134.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Among 415 patients with parkinsonism, 16 (3.9%) had findings of progressive supranuclear palsy (PSP). This report reviews the clinical features and response to drug therapy in those 16 patients. Anticholinergic drugs failed to benefit any of the 5 patients treated, while presynaptic dopaminergic drugs (Sinemet or amantadine) were beneficial in only 5 of 22 patient trials. Alternatively, dopamine agonists (bromocriptine and pergolide) caused improvement in 9 of 14 patient trials, despite the fact that all but 1 of these patients had previously failed to respond to presynaptic dopaminergic drugs. Dopamine agonists such as bromocriptine and pergolide may be useful in some patients with PSP.

L9 ANSWER 312 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 238
ACCESSION NUMBER: 1983:605969 CAPLUS
DOCUMENT NUMBER: 99:205969
ORIGINAL REFERENCE NO.: 99:31532h,31533a
TITLE: Therapeutic potentials of centrally acting dopamine and α 2-adrenoreceptor agonists
AUTHOR(S): Goldstein, M.; Engel, J.; Lieberman, A.; Regev, I.; Bystritsky, A.; Mino, S.
CORPORATE SOURCE: Med. Cent., New York Univ., New York, NY, 10016, USA
SOURCE: Journal of Neural Transmission, Supplement (1983), 18(Basic Aspects Recept. Biochem.), 257-63
CODEN: JNTSD4; ISSN: 0303-6995
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The semisynthetic ergoline pergolide [66104-22-1], the partial ergoline LY 141865 [80373-22-4], and the 8- α -aminoergoline CU 32-085 [72786-12-0] were effective antitremor agents in monkeys with ventromedial tegmental lesions. The administration of pergolide or LY 141865 results in a relief of tremor with a concomitant occurrence of severe abnormal involuntary movements, whereas the administration of CU 32-085 results in a relief of tremor with the occurrence of only minor abnormal involuntary movements. Clin. studies revealed that pergolide is an effective drug in patients with advanced Parkinson's disease, and it reduces the on-off phenomena. The possible regulation of dopamine [51-61-6] neurotransmission by the norepinephrine [51-41-2] neuronal systems was reviewed. Preliminary data suggest that clonidine [4205-90-7] may interact with presynaptic dopamine receptors.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L9 ANSWER 313 OF 331 MEDLINE on STN DUPLICATE 239
ACCESSION NUMBER: 1983227592 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6858770
TITLE: The effects of pergolide on the cardiovascular system of 40 patients with Parkinson's disease.
AUTHOR: Leibowitz M; Lieberman A N; Neophytides A; Gopinathan G; Goldstein M
SOURCE: Advances in neurology, (1983) Vol. 37, pp. 121-30.
Journal code: 0367524. ISSN: 0091-3952.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198307
ENTRY DATE: Entered STN: 19 Mar 1990
Last Updated on STN: 19 Mar 1990
Entered Medline: 8 Jul 1983

AB The effect of pergolide, a semisynthetic ergot alkaloid, on the cardiovascular system of 40 patients with Parkinson's disease (PD) was evaluated. The mean daily dose of pergolide was 2.4 mg (range, 0.1 to 10 mg). The mean duration of follow-up was 6 months (range, 2 weeks to 20 months). The 40 patients were selected only on the basis of severe PD. All 13 patients in the first part of the study underwent 1 to 5 days of Holter monitoring before starting pergolide. Monitoring was then carried out for an additional period of between 2 and 10 weeks while the patients were on pergolide. Seven of the 13 patients manifested repetitive ventricular rhythms. These were isolated and unassociated with increases in premature ventricular contractions. The dose at which the RVRs occurred was a function of the presence or absence of heart disease. The changes occurred below 3 mg/day in patients with heart disease and above 3 mg/day in patients without heart disease. Pergolide was discontinued in three of the patients with heart disease. It was concluded that pergolide may, in the diseased heart, predispose to RVRs. In the second part of the study, Holter monitoring was carried out only at the discretion of the cardiologist, and five patients were so monitored. None of these patients was rejected from the study. Only one patient (with heart disease) of the 27 patients in the second part of the study experienced an arrhythmia. This consisted of an increase in PVCs on 4 mg/day of pergolide. Pergolide was discontinued. Eight of the 40 patients in these early dose-ranging studies experienced orthostasis, two with syncope, immediately on addition of pergolide (0.1 to 0.4 mg) to levodopa. The orthostasis could be eliminated in all but two patients by reducing or discontinuing levodopa.

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ACCESSION NUMBER: 1983:317468 BIOSIS
DOCUMENT NUMBER: PREV198376074960; BA76:74960
TITLE: PERGOLIDE INDUCED CIRCLING IN RATS WITH 6 HYDROXY DOPAMINE
LESIONS IN THE NIGRO STRIATAL PATHWAY.
AUTHOR(S): DUVOISIN R C [Reprint author]; HEIKKILA R E; MANZINO L
CORPORATE SOURCE: DEP NEUROL, UMDNJ-RUTGERS MED SCH, PO BOX 101, PISCATAWAY,
NJ 08854, USA
SOURCE: Neurology, (1982) Vol. 32, No. 12, pp. 1387-1391.
CODEN: NEURAI. ISSN: 0028-3878.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB In rats with a unilateral 6-hydroxydopamine lesion of the nigrostriatal system the behavioral effects of pergolide were compared with those of L-dopa, bromocriptine and lergotrile. In this animal model of parkinsonism, doses of 0.25 mg/kg pergolide (free base) induced vigorous circling for 24 h. Pergolide was more potent than bromocriptine or lergotrile. Pretreatment with α -methyl-p-tyrosine nearly abolished the effects of bromocriptine, markedly diminished the effects of lergotrile and only partially diminished the effects of pergolide. Apparently, pergolide should be more effective than bromocriptine in the treatment of parkinsonism.

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ACCESSION NUMBER: 1983:247933 BIOSIS
DOCUMENT NUMBER: PREV198376005425; BA76:5425
TITLE: FURTHER STUDIES WITH PERGOLIDE IN PARKINSON DISEASE.
AUTHOR(S): LIEBERMAN A N [Reprint author]; GOLDSTEIN M; GOPINATHAN G;
LEIBOWITZ M; NEOPHYTIDES A; WALKER R; HIESIGER E; NELSON J
CORPORATE SOURCE: 530 FIRST AVE, SUITE 5A, NEW YORK, NY 10016, USA

SOURCE: Neurology, (1982) Vol. 32, No. 10, pp. 1181-1184.
CODEN: NEURAI. ISSN: 0028-3878.

DOCUMENT TYPE: Article

FILE SEGMENT: BA

LANGUAGE: ENGLISH

AB Pergolide was administered to 56 patients with advanced Parkinson disease who were no longer satisfactorily responding to levodopa. The group included 45 patients with on-off phenomena. Pergolide, when combined with levodopa, resulted in a 44% decrease in disability as assessed in the on period, a 15% decrease in disability in the off period and a 148% increase in the number of hours in which patients were on (from 4.6 ± 0.3 to 11.4 ± 0.6 h). All these changes were significant at 1%. Of the 56 patients, 41 (59%) improved when pergolide was added to levodopa. Mean dose of pergolide was 2.5 mg (range, 0.2-10.0 mg). Mean duration of the study was 13 mo. (range, 1 day to 34 mo.). Maximum improvement occurred within 2 mo. and began to decline, usually after 6 mo. The major adverse effects necessitating discontinuing pergolide were the occurrence of an organic confusional syndrome (6 patients), increased dyskinesias (4 patients) and cardiovascular abnormalities (3 patients). Nine patients discontinued pergolide because of a lack of effect or declining effect.

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ACCESSION NUMBER: 1983:247932 BIOSIS

DOCUMENT NUMBER: PREV198376005424; BA76:5424

TITLE: PERGOLIDE MESYLATE AND IDIOPATHIC PARKINSON DISEASE.

AUTHOR(S): TANNER C M [Reprint author]; GOETZ C G; GLANTZ R H; GLATT S L; KLAUANS H L

CORPORATE SOURCE: DEP NEUROLOGICAL SCI, RUSH-PRESBYTERIAN-ST LUKE'S MED CENT, 1725 W HARRISON, CHICAGO, ILL 60612, USA

SOURCE: Neurology, (1982) Vol. 32, No. 10, pp. 1175-1179.

CODEN: NEURAI. ISSN: 0028-3878.

DOCUMENT TYPE: Article

FILE SEGMENT: BA

LANGUAGE: ENGLISH

AB The effects of pergolide mesylate were studied in an open trial of 23 patients with idiopathic Parkinson disease (PD). All had suffered from loss of efficacy or dose-limiting side effects on current antiparkinsonian regimens. On pergolide therapy, improvement, which was maintained for 6 mo., was noted in some parkinsonian features in all 23 patients. All patients suffering from on-off phenomenon were helped by pergolide. Significant side effects were not encountered. Pergolide is useful in the treatment of PD.

L9 ANSWER 317 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1982:1401 TOXCENTER

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DOCUMENT NUMBER: 20-05654

TITLE: Cholinergic and dopaminergic mechanisms in Parkinson's disease after long term levodopa administration

AUTHOR(S): Yahr, M. D.; Clough, C. G.; Bergmann, K. J.

CORPORATE SOURCE: Clin. Ctr. for Res. in Parkinson's and Allied Disorders, Mt. Sinai School of Med., New York, NY 10029

SOURCE: Lancet (England), (Sep 25 1982) Vol. 2, pp.

709-710. 3 Refs.

CODEN: LANCAO. ISSN: 0023-7507.

DOCUMENT TYPE: Letter

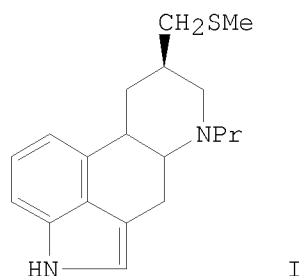
FILE SEGMENT: IPA

OTHER SOURCE: IPA 82:4830

LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB The cholinergic and dopaminergic mechanisms in Parkinson disease were investigated in 19 patients who developed fluctuating therapy responses during long term therapy with Sinemet (I; carbidopa, combination, levodopa) alone (7 patients) and I plus bromocriptine or pergolide (14 patients). Results showed random fluctuations during the on-off and end-start dose. A return of cholinergic supersensitivity and of denervation supersensitivity reactive to endogenous fluctuating levels of acetylcholine following long term levodopa administration is suggested.
Lilia M. Sancho

L9 ANSWER 318 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 243
ACCESSION NUMBER: 1983:65337 CAPLUS
DOCUMENT NUMBER: 98:65337
ORIGINAL REFERENCE NO.: 98:9861a,9864a
TITLE: Degree of selectivity of pergolide as an agonist at presynaptic versus postsynaptic dopamine receptors: implications for prevention or treatment of tardive dyskinesia
AUTHOR(S): Fuller, Ray W.; Clemens, James A.; Hynes, Martin D., III
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Journal of Clinical Psychopharmacology (1982), 2(6), 371-5
CODEN: JCPYDR; ISSN: 0271-0749
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB pergolide (I) [66104-22-1] is a potent dopamine [51-61-6] agonist that is being evaluated clin. in Parkinson's disease, hyperprolactinemia, and other diseases. I activates both presynaptic and postsynaptic dopamine receptors, with some apparent selectivity for the presynaptic dopamine autoreceptors. In rats, low doses of I mesylate (≤ 0.01 mg/kg, i.p.) decreased dopamine turnover in brain, decreased serum prolactin [9002-62-4] concentration, and reduced blood pressure in spontaneously hypertensive rats. At somewhat higher doses (≥ 0.05 mg/kg, i.p.), I caused contralateral turning in nigrostriatal-lesioned rats, elevation of serum corticosterone [50-22-6], and hypermotility with stereotyped behavior. All of these actions appear to be due to stimulation of dopamine receptors at various sites, but I may have preferential affinity for presynaptic dopamine receptors. If low doses of

I can reduce dopaminergic transmission by activating presynaptic receptors that control dopamine release, then this action might be therapeutically useful in treating schizophrenia without causing tardive dyskinesia or in the treatment of tardive dyskinesia.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD
(4 CITINGS)

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ACCESSION NUMBER: 1983:224745 BIOSIS
DOCUMENT NUMBER: PREV198375074745; BA75:74745
TITLE: LOCO MOTOR HYPO KINESIA IN THE RESERPINE TREATED RAT DRUG
EFFECTS FROM THE CORPUS STRIATUM AND NUCLEUS ACCUMBENS.
AUTHOR(S): JOHNELS B [Reprint author]
CORPORATE SOURCE: DEP OF NEUROL, UNIV OF GOTEBOG, GOTEBOG, SWEDEN
SOURCE: Pharmacology Biochemistry and Behavior, (1982)
Vol. 17, No. 2, pp. 283-290.
CODEN: PBBHAU. ISSN: 0091-3057.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB A mechanographic method was used to assess the locomotor performance induced by apomorphine or other dopaminergic drugs in reserpine-treated rats. Reserpine induced locomotor hypokinesia. The hypokinesia was dose-dependently reversed by apomorphine (APO), bromocriptine and pergolide. Locomotion was induced by microinjection of APO into the nucleus accumbens. No locomotor effect was found after injection into corpus striatum. Injection into both nuclei was not superior to accumbens only. Intra-striatal or intraaccumbens injections of trifluoperazine blocked the effect on locomotion by systematic apomorphine. Evidently reserpine-induced locomotor hypokinesia is reversed by dopaminergic stimulation in the nucleus accumbens. Blockade of striatal or accumbens' dopamine receptors may counteract apomorphine-induced locomotion, presumably by interaction with postural motor control. Evidence was found for separate dopaminergic control of locomotion and muscle tone. This may be of importance for the development of new antiparkinson drugs.

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ACCESSION NUMBER: 1982200915 EMBASE
TITLE: Pergolide in late-stage Parkinson disease.
AUTHOR: Lang, A.E.; Quinn, N.; Brincat, S.; et. al.
CORPORATE SOURCE: Univ. Dept. Neurol., Inst. Psychiatry, London SE5 8AF,
United Kingdom.
SOURCE: Annals of Neurology, (1982) Vol. 12, No. 3, pp.
243-247.
ISSN: 0364-5134 CODEN: ANNED3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 020 Gerontology and Geriatrics
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Dec 1991
Last Updated on STN: 9 Dec 1991

AB Twenty-six patients with late-stage Parkinson disease were given 0.4 to 15 mg of pergolide mesylate daily in addition to, or as replacement for, levodopa or bromocriptine therapy. Despite treatment with individually determined optimum doses of levodopa, bromocriptine, and anticholinergics, they had shown response failure or fluctuating response. Forty percent (11 patients) were unable to tolerate pergolide. Nausea and vomiting, somnolence, and psychiatric disturbances were the

most frequent side effects. Eleven of the remaining patients improved on pergolide, 2 were unchanged, and 2 were slightly worse. Among the patients who benefited, pergolide improved dose-related response fluctuations more than non-dose-related fluctuations, with a reduction in number and duration of 'off' periods and improvement in quality of sleep and early morning akinesia but little change in freezing episodes. Despite treatment failure in many cases, pergolide is at present the best available drug for specific late-stage management problems.

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ACCESSION NUMBER: 1983:178644 BIOSIS
DOCUMENT NUMBER: PREV198375028644; BA75:28644
TITLE: USE OF PERGOLIDE A POTENT DOPAMINE AGONIST IN PARKINSONS
DISEASE.
AUTHOR(S): LIEBERMAN A N [Reprint author]; NEOPHYTIDES A; LEIBOWITZ M;
GOPINATHAN G; WALKER R; PACT V; GOLDSTEIN M
CORPORATE SOURCE: 530 FIRST AVE, SUITE 5A, NEW YORK, NY 10016, USA
SOURCE: Clinical Pharmacology and Therapeutics, (1982)
Vol. 32, No. 1, pp. 70-75.
CODEN: CLPTAT. ISSN: 0009-9236.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Pergolide, a semisynthetic ergoline and a potent long-acting
adenylate cyclase-linked dopamine agonist, was given to 40 patients with
advanced Parkinson's disease whose response to L-dopa had
diminished considerably. The group included 31 patients with marked
diurnal oscillations in performance (wearing off and/or on-off phenomena).
Pergolide alone (7 patients) or combined with L-dopa (33 patients)
resulted in a reduction in disability ($P \leq 0.01$) as assessed in
both the patients' on and off periods. Pergolide also resulted
in an increase ($P \leq 0.001$) in the number of hours in which patients
were on from 3.8 (± 0.4) to 11.9 (± 0.9). The mean daily dose of
pergolide was 2.4 mg (0.1-10.0). The mean duration of the study
was 12 mo. (1-24). Pergolide is effective in Parkinson
's disease and will change the management of patients whose response to
L-dopa has diminished.

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ACCESSION NUMBER: 1982138611 EMBASE
TITLE: [Dopamine-receptor stimulants in the treatment of
Parkinson's disease].
DOPAMINREZEPTOREN-STIMULATOREN IN DER BEHANDLUNG DER
PARKINSONKRANKHEIT.
AUTHOR: Ringwald, E.; Hirt, D.; Markstein, R.; Vigouret, J.M.
CORPORATE SOURCE: Praklin. Klin. Forsch. Abt., Sandoz A.G., 4002 Basel,
Switzerland.
SOURCE: Nervenarzt, (1982) Vol. 53, No. 2, pp. 67-71.
ISSN: 0028-2804 CODEN: NERVAF
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: German
ENTRY DATE: Entered STN: 9 Dec 1991
Last Updated on STN: 9 Dec 1991

AB Following the successful introduction of a dopamine agonist,
bromocriptine, into the treatment of Parkinson's disease,
pharmaceutical research has developed other substances with a similar

action-profile. The theoretical basis of dopamine-receptor stimulation in the Parkinson syndrome is described. Concise reference is made to the pharmacology and clinical effects of the drugs so far subjected to clinical trials (bromocriptine, CM 29-712, CF 25-397, CQ 32-084, CU 32-085, lergotriple, lisuride and pergolide). Of these, CU 32-085 appears to be tolerated best, with good efficacy. The role of the dopamine receptor-stimulating substances in addition to L-dopa in the treatment of Parkinson's syndrome, is emphasized and argued.

L9 ANSWER 323 OF 331 DISSABS COPYRIGHT (C) 2009 ProQuest Information and Learning Company; All Rights Reserved on STN

ACCESSION NUMBER: 81:21311 DISSABS Order Number: AAR8117702

TITLE: INTERACTION OF AGENTS WITH DOPAMINE AND SEROTONIN NEUROTRANSMITTER SYSTEMS

AUTHOR: ROSENFELD, MYRNA RACHEL [PH.D.]

CORPORATE SOURCE: YESHIVA UNIVERSITY (0266)

SOURCE: Dissertation Abstracts International, (1981) Vol. 42, No. 3B, p. 984. Order No.: AAR8117702. 193 pages.

DOCUMENT TYPE: Dissertation

FILE SEGMENT: DAI

LANGUAGE: English

ENTRY DATE: Entered STN: 19921118

Last Updated on STN: 19921118

AB The interaction of several neuroactive agents with the dopaminergic and serotonergic neurotransmitter systems in mammalian brain was studied. Two approaches were taken: (1)the effect of the agents on dopamine and serotonin stimulated adenylate cyclase and (2)the ability of the compounds to bind directly to dopamine or serotonin receptor sites. The compounds of particular interest were the ergot derivatives lisuride and pergolide and the neuroleptic agent, molindone. All of these compounds have been used clinically for the treatment of disorders such as migraine, Parkinson's disease and psychotic illness.

Studies were carried out using rabbit or rat brain. Adenylate cyclase activity was studied in crude homogenates. Cyclic AMP levels were determined with a protein binding assay. Direct receptor binding studies were performed on washed tissue homogenates.

Adenylate cyclase activity was studied in three brain regions, frontal cortex, anterior limbic cortex and caudate nucleus of the rabbit and in the striatum of rat. Serotonin-sensitive adenylate cyclase was found in both cortical regions but not in caudate. Dopamine-sensitive adenylate cyclase was found in all regions. The cortical dopamine-sensitive adenylate cyclase was distinguished from the activity in caudate by its greater sensitivity to the dopamine analog, ADTN.

Lisuride was found to be an extraordinarily potent stimulator of serotonin-stimulated adenylate cyclase. Lisuride produced significant stimulations at concentrations as low as 10^{-9} M. Pergolide stimulated dopamine-sensitive adenylate cyclase in rat striatum. Lisuride, lergotriple and bromocriptine were inactive in stimulating the dopamine-sensitive adenylate cyclase.

Molindone was shown to be a rather selective antagonist of serotonin-stimulated adenylate cyclase and was used as a tool to study the interaction of lisuride and the other ergots with adenylate cyclase. In addition, the effect of $1 (\mu)$ M GTP on the ability of the ergots to interact with dopamine-sensitive adenylate cyclase in rat striatum was investigated. This concentration of GTP enhanced the stimulation produced by pergolide while having no effect on lisuride, lergotriple or bromocriptine.

The ability of lisuride and molindone to interact with dopamine and serotonin receptor sites in rabbit frontal cortex and caudate nucleus and rat striatum was studied. Ligands used to study serotonin receptors in cortex were $\{(^3\text{H})\}$ serotonin, $\{(^3\text{H})\}$ spiroperidol and $\{(^3\text{H})\}$ LSD. Serotonergic sites in caudate were studied with $\{(^3\text{H})\}$ serotonin and

dopaminergic sites with $\{(^3\text{H})\text{ADTN}\}$. $\{(^3\text{H})\text{LSD}\}$ binding in caudate was shown to be to both dopamine and serotonin receptor sites. Lisuride could bind to serotonergic sites in cortex and both dopaminergic and serotonergic sites in caudate nucleus with IC_{50} 's in the nM range. Furthermore, the interaction of lisuride at serotonergic sites in frontal cortex was determined to be that of an agonist by the sensitivity of this interaction to the guanine nucleotide analog Gpp(NH)p.

In contrast, molindone interacted weakly with all receptor binding sites studied. Both lisuride and molindone interacted non-selectively with the serotonin and dopamine subcomponents of $\{(^3\text{H})\text{LSD}\}$ binding in rabbit caudate nucleus. Lisuride and molindone were shown to interact with both guanine nucleotide sensitive and insensitive $\{(^3\text{H})\text{ADTN}\}$ and $\{(^3\text{H})\text{serotonin}\}$ binding sites. Lisuride showed a slight preference for the nucleotide sensitive sites of both of these ligands. Molindone interacts preferentially with the nucleotide sensitive component of $\{(^3\text{H})\text{serotonin}\}$ binding. The effect of ions and different tissue preparations of receptor binding was also investigated.

Lisuride is shown to interact with both serotonin receptors coupled to adenylate cyclase and with serotonin receptors not coupled to adenylate cyclase. While lisuride does not stimulate dopamine-sensitive adenylate cyclase it can interact with dopamine receptor sites. Molindone is demonstrated to be a selective antagonist of serotonin-stimulated adenylate cyclase. In contrast to other neuroleptic agents, molindone is not selective for dopamine-coupled adenylate cyclase receptors but rather has weak interactions with both adenylate cyclase coupled and non-coupled dopamine receptors.

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STN DUPLICATE 247

ACCESSION NUMBER: 1982:219980 BIOSIS
DOCUMENT NUMBER: PREV198273079964; BA73:79964
TITLE: CARDIAC EFFECTS OF PERGOLIDE.
AUTHOR(S): LEIBOWITZ M [Reprint author]; LIEBERMAN A; GOLDSTEIN M;
NEOPHYTIDES A; KUPERSMITH M; GOPINATHAN G; MEHL S
CORPORATE SOURCE: 907 FIFTH AVE, NEW YORK, NY 10016, USA
SOURCE: Clinical Pharmacology and Therapeutics, (1981)
Vol. 30, No. 6, pp. 718-723.
CODEN: CLPTAT. ISSN: 0009-9236.

DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The effect of pergolide, a semisynthetic ergot alkaloid, alone or combined with carbidopa and levodopa (Sinemet), was examined on the cardiac rhythm of 12 patients with Parkinson's disease. The patients were selected on the basis of severe Parkinson's disease and stable cardiac rhythm as determined by 1-5 days of Holter monitoring. Monitoring was carried out for an additional period of 2-10 wk while the patients were on pergolide. Of the 12 patients, 7 had repetitive ventricular rhythms (RVR). These were isolated, infrequent and not associated with increases in premature ventricular contractions. The dose at which the RVR occurred may be a function of the presence or absence of heart disease, but the significance of RVR remains to be determined.

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ACCESSION NUMBER: 1981:1530 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 19-03826
TITLE: Cardiac effects of pergolide
AUTHOR(S): Leibowitz, M.; Lieberman, A.; Goldstein, M.; Neophytides, A.; Kupersmith, M.; et al
CORPORATE SOURCE: 907 Fifth Ave., New York, NY 10016

SOURCE: Clinical Pharmacology and Therapeutics (USA), (Dec 1981) Vol. 30, pp. 718-723. 25 Refs.
CODEN: CLPTAT. ISSN: 0009-9236.

DOCUMENT TYPE: Journal

FILE SEGMENT: IPA

OTHER SOURCE: IPA 81:4816

LANGUAGE: English

ENTRY DATE: Entered STN: 16 Nov 2001

Last Updated on STN: 16 Nov 2001

AB The effect of pergolide mesylate (I), 0.1-5.0 mg daily, alone or combined with carbidopa and levodopa (Sinemet), on cardiac rhythm was examined in 18 patients with Parkinson's disease. Patients were selected on the basis of severe Parkinson's disease and stable cardiac rhythm as determined by one to 5 days of Holter monitoring. Monitoring was then carried out for an additional period of between 2 and 10 wk while the patients were on I. Fifty-eight per cent of 12 patients studied had repetitive ventricular rhythms while undergoing treatment with I. These were isolated, infrequent, and not associated with increases in premature ventricular contractions. The significance of the repetitive ventricular rhythms were not determined. It was recommended that dosages above 3 mg of I be used with caution in patients with heart disease.

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ACCESSION NUMBER: 1981:284018 BIOSIS

DOCUMENT NUMBER: PREV198172069002; BA72:69002

TITLE: TREATMENT OF ADVANCED PARKINSON DISEASE WITH PERGOLIDE.

AUTHOR(S): LIEBERMAN A [Reprint author]; GOLDSTEIN M; LEIBOWITZ M;
NEOPHYTIDES A; KUPERSMITH M; PACT V; KLEINBERG D

CORPORATE SOURCE: NYU MED CENT, 530 FIRST AVE, SUITE 5A, NEW YORK, NY 10016,
USA

SOURCE: Neurology, (1981) Vol. 31, No. 6, pp. 675-682.

CODEN: NEURAI. ISSN: 0028-3878.

DOCUMENT TYPE: Article

FILE SEGMENT: BA

LANGUAGE: ENGLISH

AB Pergolide mesylate, a semisynthetic ergoline and a potent, long-acting central dopamine agonist, was tested in 13 patients with advanced Parkinson disease and diurnal oscillations in performance (wearing-off or on-off phenomena or both) whose response to L-dopa had diminished considerably. Among all 9 patients who completed the initial clinical trial, pergolide alone (2 patients) or combined with L-dopa (7 patients) had a marked antiparkinsonian effect. There was a significant reduction in rigidity, bradykinesia, gait disorder and total Parkinson disease disability score. Pergolide had a marked effect in all the patients with wearing-off or on-off phenomena or both, resulting in a significant increase in the duration of the time patients were on. The number of hours in which patients were on increased from 3.8 ± 0.5 (SE) to 11.4 ± 0.08 (SE). The mean daily dose of pergolide was 2.4 mg (range, 2-5 mg). At 10 mo. later, all 9 patients were doing well. Pergolide is an effective drug in patients with advanced Parkinson disease and reduces on-off phenomena.

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ACCESSION NUMBER: 1981213004 EMBASE

TITLE: Pergolide and lisuride for levodopa-induced oscillations.

AUTHOR: Lees, A.J.; Stern, G.M.

CORPORATE SOURCE: Dept. Neurol., Univ. Coll. Hosp., London WC1, United
Kingdom.

SOURCE: Lancet, (1981) Vol. 2, No. 8246, pp. 577.

ISSN: 0140-6736 CODEN: LANCAO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Dec 1991
Last Updated on STN: 9 Dec 1991

AB We describe here preliminary results of separate trials of two new ergoline derivatives, lisuride and pergolide. These studies confirm previous reports showing that both drugs possess anti-parkinsonian properties which can smoothe out oscillations in certain patients. Pergolide is more effective and its longer duration of action (4-8 h compared with 1-3 h for lisuride) probably contributes to its superiority in alleviating end-of-dose akinesia. Despite pergolide's striking effects in potentiating the levodopa response, intolerable dyskinesia marred long-term efficacy in six patients.

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ACCESSION NUMBER: 1982:167007 BIOSIS
DOCUMENT NUMBER: PREV198273026991; BA73:26991
TITLE: PHYSIOLOGIC DISPOSITION OF PERGOLIDE.
AUTHOR(S): RUBIN A [Reprint author]; LEMBERGER L; DHAHIR P
CORPORATE SOURCE: LILLY LAB CLIN RES, ELI LILLY AND CO, WISHARD MEML HOSP,
1001 W 10TH ST, INDIANAPOLIS, INDIANA 46202, USA
SOURCE: Clinical Pharmacology and Therapeutics, (1981)
Vol. 30, No. 2, pp. 258-265.
CODEN: CLPTAT. ISSN: 0009-9236.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Pergolide, a synthetic ergoline, is a potent long-acting dopaminergic drug effective in Parkinson's disease and amenorrhea-galactorrhea. After 138 μ g 14 C- pergolide orally to healthy subjects, radioactivity was present in plasma and red blood cells. Salivary radioactivity was 1/3-1/10 that in plasma. Radioactivity in plasma appeared after 15-30 min, peaked at 1-2 h and was barely detectable after 96 h. Plasma radioactivity was not attributable to pergolide and the levels did not correlate well with the duration of the prolactin-lowering effect induced by pergolide. Pergolide became bound to several plasma proteins and could not be displaced by other drugs that are also bound or by possible metabolites of pergolide. Radioactivity was eliminated as pergolide metabolites in urine (55%), feces (40%) and breath (5%, as 14 CO₂).

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ACCESSION NUMBER: 1980:267433 BIOSIS
DOCUMENT NUMBER: PREV198070059929; BA70:59929
TITLE: INTERACTION OF PERGOLIDE WITH CENTRAL DOPAMINERGIC RECEPTORS.
AUTHOR(S): GOLDSTEIN M [Reprint author]; LIEBERMAN A; LEW J Y; ASANO T; ROSENFELD M R; MAKMAN M H
CORPORATE SOURCE: DEP PSYCHIATRY, NY UNIV MED CENT, 560 FIRST AVE, NEW YORK, NY 10016, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1980) Vol. 77, No. 6, pp. 3725-3728.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article

FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The activity of pergolide, an N-propylergoline derivative, was tested for stimulation of central dopaminergic receptors. Binding to dopamine receptors shows that pergolide acts as an agonist with respect to the receptors. GTP decreases the potencies of dopamine agonists and of pergolide, but not of bromocriptine, to displace [3H]spiroperidol ([3H]Spi) from striatal membrane sites. The GTP-sensitive site labeled by [3H]Spi seems to be localized on intrastriatal dopamine receptors. The potency of dopamine agonists and of pergolide to displace [3H]Spi from striatal receptor sites is reduced in membranes exposed to higher temperatures. Pergolide, but not dopaminergic ergots, stimulates dopamine-sensitive adenylate cyclase in striatal homogenates. Pergolide, unlike other dopaminergic ergots, acts as an agonist on GTP-sensitive components of [3H]Spi binding and stimulates dopamine receptors linked to dopamine-sensitive adenylate cyclase. The drug induces turning behavior in rats with 6-OH-dopamine lesions and relieves tremor in monkeys [*Cercopithecus sabaues*] with ventromedial tegmental lesions for a longer time at a lower dose than other tested dopaminergic ergots. Other studies show that it is effective in the treatment of patients with advanced parkinsonism.

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ACCESSION NUMBER: 1981:142327 BIOSIS
DOCUMENT NUMBER: PREV198171012319; BA71:12319
TITLE: THE PHARMACOLOGICAL EVALUATION OF PERGOLIDE MESYLATE AS A
POTENTIAL ANTI PARKINSON AGENT.
AUTHOR(S): KOLLER W C [Reprint author]; WEINER W J; DIAMOND B I;
NAUSIEDA P A; KLAWANS H L
CORPORATE SOURCE: DEP NEUROL SCI, RUSH-PRESBYT ST LUKE'S MED CENT, 1725 W
HARRISON, CHICAGO, ILL 60612, USA
SOURCE: Neuropharmacology, (1980) Vol. 19, No. 9, pp.
831-838.
CODEN: NEPHBW. ISSN: 0028-3908.

DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The effects of the putative dopamine agonist, pergolide mesylate, a substituted propylergoline, were investigated in several animal models of dopamine-related behavior in an attempt to evaluate its possible role in the treatment of Parkinsonism. Pergolide induced intense stereotypic behavior in both rats and guinea-pigs. The stereotypy was immediate in onset, of prolonged duration, and was blocked by non-sedating doses of haloperidol but not by clozapine. In rats, pergolide reversed reserpine-induced effects even in animals pretreated with the dopamine depletor, α -methyl-p-tyrosine. Pergolide induced vomiting in dogs which could be inhibited by pretreatment with haloperidol. In animals with unilateral 6-hydroxydopamine lesions of the substantia nigra, pergolide produced contralateral rotation. Behavioral subsensitivity to apomorphine developed after 4 wk of chronic administration of a low (subthreshold) dose of pergolide that did not induce stereotyped behavior, while supersensitivity to apomorphine was observed when animals were chronically treated with a suprathreshold dose of pergolide. Pergolide can cause stimulation of central dopaminergic receptors and possesses direct agonist properties. However pergolide does have effects which are different from those of other available dopaminergic drugs and may be advantageous in the treatment of Parkinson's disease.

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STN DUPLICATE 253

ACCESSION NUMBER: 1980:267291 BIOSIS
DOCUMENT NUMBER: PREV198070059787; BA70:59787
TITLE: PERGOLIDE MESYLATE A POTENT DAY LONG INHIBITOR OF PROLACTIN
IN RHESUS MONKEYS AND PATIENTS WITH PARKINSONS DISEASE.
AUTHOR(S): KLEINBERG D L [Reprint author]; LIEBERMAN A; TODD J;
GREISING J; NEOPHYTIDES A; KUPERSMITH M
CORPORATE SOURCE: NY VETERANS ADM MED CENT, 408 FIRST AVE, NEW YORK, NY
10010, USA
SOURCE: Journal of Clinical Endocrinology and Metabolism, (
1980) Vol. 51, No. 1, pp. 152-154.
CODEN: JCEMAZ. ISSN: 0021-972X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The effect of a new synthetic ergot alkaloid, pergolide mesylate
[PM] on the inhibition of PRL [prolactin] during 24-h periods was
evaluated in 4 rhesus monkeys and 3 patients with Parkinson's
disease. In the monkeys, the mean PRL level during the 24-h period fell
to 24% of control in response to 50 µg PM daily and to 6.6% of control
with 200 µg. With 1000 µg PM daily, PRL was unmeasurable in the
great majority of samples over 24 h. In addition, the marked episodic
fluctuation in PRL occurring in controls was not observed in treated
animals. In 3 patients with Parkinson's disease, treatment with
PM also resulted in uniform 24-h suppression of PRL. In 1 patient on PM
(100 µg/day), the mean 24-h PRL level fell to 18% of control, and in 2
other patients on 200 and 600 µg PM, respectively, whose mean PRL
levels were 4.1 and 7.4 ng/ml, respectively, before treatment, no PRL was
detected in any of the blood samples obtained during the 24-h periods. PM
apparently is a potent inhibitor of PRL in rhesus monkeys and in patients
with Parkinson's disease; the effect is uniform over 24-h
periods.

=> FIL STNGUIDE

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MEDLINE, SCISEARCH, TOXCENTER' - CONTINUE? (Y)/N:Y

L9 ANSWER 21 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 16

ACCESSION NUMBER: 2002:260796 BIOSIS
DOCUMENT NUMBER: PREV200200260796

TITLE: Rapid-eye-movement sleep disorders in Parkinson's disease.
Original Title: Les troubles du sommeil paradoxal dans la
maladie de Parkinson.
AUTHOR(S): Gagnon, J.-F.; Montplaisir, J.; Bedard, M.-A. [Reprint
author]
CORPORATE SOURCE: Unite des Troubles du Mouvement Andre Barbeau, Hotel-Dieu,
CHUM, 3840, rue St-Urbain, Montreal, Quebec, H2W 1T8,
Canada
bedard.marc-andre@uqam.ca
SOURCE: Revue Neurologique (Paris), (Fevrier, 2002) Vol.
158, No. 2, pp. 135-152. print.
CODEN: RENEAM. ISSN: 0035-3787.
DOCUMENT TYPE: Article
LANGUAGE: French
ENTRY DATE: Entered STN: 24 Apr 2002
Last Updated on STN: 24 Apr 2002

AB During the past 10 years, there has been an increasing interest in the study of rapid-eye-movement (REM) sleep in neurodegenerative diseases and more particularly in Parkinson's disease (PD). This interest is justified by the strong association observed between these diseases and REM sleep behavior disorder (RBD). In the first section of this paper, a critical review of the literature on the presence of REM sleep disorders in PD is presented. Studies that show an association between PD and RBD are reviewed. Studies that report the presence of other REM sleep disorders in PD (short latency, abnormal length and/or proportion of REM sleep, increasing occurrence of hallucinations) are then discussed. Limitations of the criteria proposed by Rechtschaffen et Kales (1968) for the quantification of REM sleep are also presented. Some authors believe that dopaminergic (DA) agents used in the treatment of PD (levodopa, bromocriptine, pergolide, pramipexole and selegiline) could be a responsible factor for the occurrence of REM sleep disorders observed in this disease. The literature concerning the impact of these DA agents on human REM sleep is therefore critically reviewed. It is concluded that DA agents cannot explain on their own the presence of REM sleep disorders in PD. Other causes, among which the disturbance of some neurochemical systems linked to the neuropathological process of the disease, must be considered in order to explain these REM sleep disorders. In the second section of this paper, we present the different pathophysiological hypotheses proposed to explain REM sleep disorders in PD, such as a dysfunction of the cholinergic, noradrenergic, serotonergic, dopaminergic or GABAergic neurons. Emphasis is placed on the role of cholinergic neurons of the pedunculopontine and laterodorsal tegmental nuclei, structures shown to be particularly impaired in PD. Neurophysiological, neuroanatomical and neuropharmacological studies demonstrate that these neurons are strongly implicated in the different REM sleep parameters (muscular atonia, electroencephalographic desynchronisation, ponto-geniculo-occipital spikes). Finally, future research directions are proposed.

L9 ANSWER 22 OF 331 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation
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ACCESSION NUMBER: 2003:47415 SCISEARCH
THE GENUINE ARTICLE: 630YW
TITLE: Pergolide mesilate may improve fatigue in patients with
Parkinson's disease
AUTHOR: Abe K (Reprint); Takanashi M; Yanagihara T; Sakoda S
CORPORATE SOURCE: Osaka Univ, Grad Sch Med, Dept Neurol, Suita, Osaka
5650871, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: BEHAVIOURAL NEUROLOGY, (2002) Vol. 13, No. 3-4,
pp. 117-121.
ISSN: 0953-4180.

PUBLISHER: IOS PRESS, NIEUWE HEMWEG 6B, 1013 BG AMSTERDAM,
NETHERLANDS.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 19

ENTRY DATE: Entered STN: 24 Jan 2003

Last Updated on STN: 24 Jan 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Objectives: Fatigue is a complaint frequently encountered among patients with Parkinson's disease (PD). Considering the possible relationship between fatigue and dopaminergic dysfunction, we investigated the effect of pergolide mesilate (a D2 and D1 dopamine receptor agonist) and bromocriptine (a D2 selective dopamine receptor) in patients with PD. Methods: We evaluated 41 patients with PD and controls. We assessed the degree of fatigue by using a fatigue scale. The severity of PD was evaluated by the Hoehn and Yahr Scale and the unified Parkinson's disease rating scale (UPDRS). Results: After five weeks from prescription, patients taking pergolide mesilate showed significant improvement in the fatigue scale (from 5.1 +/- 0.7 to 4.4 +/- 0.55, $p < 0.05$,) but patients taking bromocriptine did not (from 4.8 +/- 0.9 to 4.7 +/- 0.8). Conclusions: Our study suggested the possibility of functional correlation between fatigue and D1 receptor in patients with PD.

L9 ANSWER 23 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 17

ACCESSION NUMBER: 2002450024 EMBASE

TITLE: Neuroleptic malignant-like syndrome after rapid switch from bromocriptine to pergolide.

AUTHOR: Reimer, Jens; Kuhlmann, Anita; Muller, Thomas
(correspondence)

CORPORATE SOURCE: Department of Neurology, St. Josef Hospital, Ruhr University Bochum, Gudrunstrasse 56, 44791 Bochum, Germany.
thomas.mueller@ruhr-uni-bochum.de

AUTHOR: Muller, Thomas (correspondence)

CORPORATE SOURCE: Department of Neurology, St. Josef Hospital, Ruhr University, Gudrunstrasse 56, 44791 Bochum, Germany.
thomas.mueller@ruhr-uni-bochum.de

SOURCE: Parkinsonism and Related Disorders, (Dec 2002)
Vol. 9, No. 2, pp. 115-116.
Refs: 14

ISSN: 1353-8020 CODEN: PRDIFO

PUBLISHER IDENT.: S 1353-8020(01)00045-1

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 3 Jan 2003

Last Updated on STN: 3 Jan 2003

AB Neuroleptic malignant-like syndrome (NMLS) occurred after rapid switch from bromocriptine to pergolide in a Parkinsonian patient. Although the underlying mechanisms are as yet obscure, we hypothesize that differences in dopamine receptor affinities between bromocriptine and pergolide may be involved. Long-term treatment with bromocriptine may thus have induced plastic changes in intracellular signal processing in the nigrostriatal system, which resulted in reduced dopaminergic efficacy of pergolide. We recommend vigilant outpatient supervision during performance of rapid

switchover from one dopamine agonist to another in advanced Parkinson's disease or in subjects with predisposing factors for onset of a neuroleptic malignant syndrome. .COPYRGT. 2002 Elsevier Science Ltd. All rights reserved.

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ACCESSION NUMBER: 2003197815 EMBASE
TITLE: [Dose build-up of pergolide in a patient with Parkinson's disease and levodopa-induced complications].
Aufdosierung von pergolid bei morbus parkinson mit beginnendem l-dopa-spatsyndrom.
AUTHOR: Hahne, M., Dr. (correspondence); Griewing, B.
CORPORATE SOURCE: Neurologische Klinik Bad Neustadt, Abt. Akutneurologie/Stroke Unit, Klinische Neuropsychologie, Von-Guttenberg-Str. 10, 97616 Bad Neustadt/Saale, Germany.
SOURCE: Neurologie und Rehabilitation, (2002) Vol. 8, No. 2, pp. 93-94.
Refs: 2
ISSN: 0947-2177 CODEN: NEREF3
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: German
SUMMARY LANGUAGE: English; German
ENTRY DATE: Entered STN: 29 May 2003
Last Updated on STN: 29 May 2003

AB Long term treatment of Parkinson's disease with levodopa often induces severe motor complications including dyskinesias and on-off-phenomena. We report a case of beginning levodopa-induced complications which could be treated successfully by slow titration of pergolide up to high doses, the levodopa dosis remaining on a constant medium level.

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ACCESSION NUMBER: 2002:138231 BIOSIS
DOCUMENT NUMBER: PREV200200138231
TITLE: Effects of pharmacological agents upon a transgenic model of Parkinson's disease in Drosophila melanogaster.
AUTHOR(S): Pendleton, Robert G. [Reprint author]; Parvez, Feroz; Sayed, Marwa; Hillman, Ralph
CORPORATE SOURCE: BioPharm Consultants, 1312 Sumneytown Pike, Lower Gwynedo, PA, 19002, USA
rgp@mymailstation.com
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (January, 2002) Vol. 300, No. 1, pp. 91-96. print.
CODEN: JPETAB. ISSN: 0022-3565.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Feb 2002
Last Updated on STN: 21 Mar 2002

AB The human gene that codes for the protein alpha-synuclein has been transferred into the Drosophila melanogaster genome. The transgenic flies recapitulate some of the essential features of Parkinson's disease. These include the degeneration of certain dopaminergic neurons in the brain accompanied by the appearance of age-dependent abnormalities in locomotor activity. In the present study, we tested the locomotor response of these transgenic flies to prototypes of the major classes of drugs currently used to treat this disorder. A time course study was

first conducted to determine when impaired locomotor activity appeared relative to normal "wild-type" flies. A climbing or negative geotaxis assay measuring the ability of the organisms to climb up the walls of a plastic vial was used. Based on the results obtained, normal and transgenic flies were treated with each of the drugs in their food for 13 days and then assayed. The activity of transgenic flies treated with L-DOPA was restored to normal. Similarly, the dopamine agonists pergolide, bromocriptine, and 2,3,4,5-tetrahydro-7,8-dihydroxy-1-phenyl-1H-3-benzazepine (SK&F 38393) were substantially effective. Atropine, the prototypical muscarinic cholinergic receptor antagonist, was also effective but to a lesser extent than the other antiparkinson compounds. p-Chlorophenylalanine, an inhibitor of serotonin synthesis, was without beneficial effect as was alpha-methyl-p-tyrosine, an inhibitor of tyrosine hydroxylase, the rate-limiting step in catecholamine biosynthesis. This behavioral study further demonstrates the utility of this model in studying Parkinson's disease and reinforces the concept that inhibition of the action of alpha-synuclein may be useful in its treatment as may dopamine D1 receptor agonists.

L9 ANSWER 26 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 19

ACCESSION NUMBER: 2002:969798 CAPLUS

DOCUMENT NUMBER: 139:207543

TITLE: Both short- and long-acting D-1/D-2 dopamine agonists induce less dyskinesia than L-DOPA in the MPTP-lesioned common marmoset (*Callithrix jacchus*)

AUTHOR(S): Maratos, Eleni C.; Jackson, Michael J.; Pearce, Ronald K. B.; Cannizzaro, Carla; Jenner, Peter

CORPORATE SOURCE: Neurodegenerative Disease Res. Cent., Guy's, King's and St. Thomas' Sch. Biomed. Sci., King's College London, London, SE1 1UL, UK

SOURCE: Experimental Neurology (2002), Volume Date 2003, 179(1), 90-102

CODEN: EXNEAC; ISSN: 0014-4886

PUBLISHER: Elsevier Science

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The current concept of dyskinesia is that pulsatile stimulation of D-1 or D-2 receptors by L-DOPA or short-acting dopamine agonists is more likely to induce dyskinesia compared to long-acting drugs producing more continuous receptor stimulation. We now investigate the ability of two mixed D-1/D-2 agonists, namely pergolide (long-acting) and apomorphine (short-acting), to induce dyskinesia in drug-naïve MPTP-lesioned primates, compared to L-DOPA. Adult common marmosets (*Callithrix jacchus*) were lesioned with MPTP (2 mg/kg/day s.c. for 5 days) and subsequently treated with equieffective antiparkinsonian doses of L-DOPA, apomorphine, or pergolide for 28 days. L-DOPA, apomorphine, and pergolide reversed the MPTP-induced motor deficits to the same degree with no difference in peak response. L-DOPA and apomorphine had a rapid onset of action and short duration of effect producing a pulsatile motor response, while pergolide had a slow onset and long-lasting activity producing a continuous profile of motor stimulation. L-DOPA rapidly induced dyskinesia that increased markedly in severity and frequency over the course of the study, impairing normal motor activity by day 20. Dyskinesia in animals treated with pergolide or apomorphine increased steadily, reaching mild to moderate severity but remaining significantly less marked than that produced by L-DOPA. There was no difference in the intensity of dyskinesia produced by apomorphine and pergolide. These data suggest that factors other than duration of drug action may be important in the induction of dyskinesia but support the use of dopamine agonists in early Parkinson's disease, as a means of delaying L-DOPA therapy

and reducing the risk of developing dyskinesia.

OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS
RECORD (20 CITINGS)
REFERENCE COUNT: 89 THERE ARE 89 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 27 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights
reserved on STN DUPLICATE 20

ACCESSION NUMBER: 2002032412 EMBASE
TITLE: Chronic pericardial constriction linked to the
antiparkinsonian dopamine agonist pergolide.
AUTHOR: Balachandran, K.P.; Stewart, D.; Berg, G.A.; Oldroyd, Keith
G., Dr. (correspondence)
CORPORATE SOURCE: Department of Cardiology, Hairmyres Hospital, Eaglesham
Road, East Kilbride G75 8RG, United Kingdom. keith.oldroyd@
laht.scot.nhs.uk
SOURCE: Postgraduate Medical Journal, (2002) Vol. 78, No.
915, pp. 49-50.
Refs: 4
ISSN: 0032-5473 CODEN: PGMJAO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jan 2002
Last Updated on STN: 31 Jan 2002

AB Constrictive pericarditis is present when a fibrotic, thickened, and
adherent pericardium restricts diastolic filling of the heart. Several
drugs can cause pericarditis, which can lead to chronic pericardial
constriction. A case of constrictive pericarditis in a patient receiving
the antiparkinsonian drug pergolide is reported.

L9 ANSWER 28 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 21

ACCESSION NUMBER: 2002:227094 BIOSIS
DOCUMENT NUMBER: PREV200200227094
TITLE: Long-term studies of dopamine agonists.
AUTHOR(S): Hubble, Jean P. [Reprint author]
CORPORATE SOURCE: 1581 Dodd Drive, 371 McCampbell Hall, Columbus, OH, 43210,
USA
Hubble.5@osu.edu
SOURCE: Neurology, (February 26, 2002) Vol. 58, No. 4
Supplement 1, pp. S42-S50. print.
CODEN: NEURAI. ISSN: 0028-3878.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Apr 2002
Last Updated on STN: 3 Apr 2002

AB Dopamine agonists have long been used as adjunctive therapy for the
treatment of Parkinson's disease (PD). In more recent years
these drugs have also been proved safe and effective as initial therapy in
lieu of levodopa in the treatment of PD. Long-term levodopa therapy is
associated with motor complications, including fluctuating response
patterns and dyskinesia. By initially introducing a dopamine agonist as
symptomatic drug therapy, it may be possible to postpone the use of
levodopa and delay or prevent the development of motor complications.
Recently, four clinical trials have explored this hypothesis by comparing
the long-term response and side effects of levodopa with dopamine agonist
therapy. The drugs studied have included ropinirole, pramipexole,

cabergoline, and pergolide. In each of these projects, the occurrence of motor complications, such as wearing off and dyskinesia, was significantly less in the subjects assigned to initiation of therapy with a dopamine agonist. The addition of levodopa could be postponed by many months or even several years. Therefore, these long-term studies of dopamine agonists support the initiation of a dopamine agonist instead of levodopa in an effort to postpone levodopa-related motor complications. This therapeutic approach may be particularly appropriate in PD patients with a long treatment horizon on the basis of age and general good health. The extension phase of the long-term study comparing pramipexole with levodopa is ongoing, and follow-up information may help to establish the value of this treatment strategy.

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STN DUPLICATE 22

ACCESSION NUMBER: 2002:218534 BIOSIS

DOCUMENT NUMBER: PREV200200218534

TITLE: Validation of the French language version of the
Parkinson's Disease Questionnaire: PDQ-39.
Original Title: Validation en langue francaise d'un
questionnaire de qualite de vie dans la maladie de
Parkinson: Le Parkinson's Disease Questionnaire: PDQ-39.

AUTHOR(S): Auquier, P. [Reprint author]; Sapin, C.; Ziegler, M.;
Tison, F.; Destee, A.; Dubois, B.; Allicar, M. P.;
Thibault, J.-L.; Jenkinson, C.; Peto, V.

CORPORATE SOURCE: Laboratoire de Sante Publique, Faculte de Medecine, 27 bd
Jean Moulin, 13385, Marseille Cedex, 5, France

SOURCE: Revue Neurologique (Paris), (Janvier, 2002) Vol.
158, No. 1, pp. 41-50. print.
CODEN: RENEAM. ISSN: 0035-3787.

DOCUMENT TYPE: Article

LANGUAGE: French

ENTRY DATE: Entered STN: 27 Mar 2002

Last Updated on STN: 27 Mar 2002

AB After Alzheimer's disease, Parkinson's disease (PD) is the second most frequent degenerative disease of the central nervous system. The consequences of PD at the functional, social and emotional levels warrant a better understanding the patient's perceptions as measured using a specific instrument rather than restricting the medical approach to the clinical evaluation of the motor component. In 1996, we began implementation of a project to transculturally validate the single specific instrument that had been published and was available at that time: PDQ-39. The scale consists in a 39-item questionnaire enabling determination of an overall quality-of-life score and scores for 8 specific dimensions: mobility, activities of daily living, emotional well-being, stigma, social support, cognitions, communication and bodily discomfort. Eighty-nine patients taking part in an open-label study of the safety of a combination of pergolide and dopa therapy were included and followed up on D15 and after 8 weeks. The process of "Forward-Backward" translation, conducted in close liaison with the authors, enabled semantic and linguistic validation of the French language version. The content was validated by PD experts. At baseline, the patients presented quality-of-life scores that were particularly impaired for the dimensions exploring Mobility, Emotional well-being and Bodily discomfort. The main metric properties of the scale were confirmed. The PDQ-39 scores were closely correlated with the related concepts investigated by generic scale, SF-36. The PDQ-39 scores were correlated with the "Mental and Mood Status", "Everyday Activities" and "Motor Status" dimensions determined by the UPDRS. The reliability, expressed by Cronbach coefficients alpha, showed strong consistency of the instrument, very similar to the data for the original version. In contrast to what was observed with SF-36, the scale was particularly sensitive to clinical

changes. The initial results make PDQ-39 a precious tool for the optimization of management of patients presenting with PD.

L9 ANSWER 30 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 23
ACCESSION NUMBER: 2002:921114 CAPLUS
DOCUMENT NUMBER: 139:191160
TITLE: Dopamine Agonists Induce Episodes of Irresistible
Daytime Sleepiness
AUTHOR(S): Schlesinger, Ilana; Ravin, Paula D.
CORPORATE SOURCE: Department of Neurology, University Campus, University
of Massachusetts Memorial Health Care, Worcester, MA,
USA
SOURCE: European Neurology (2002), Volume Date 2003,
49(1), 30-33
CODEN: EUNEAP; ISSN: 0014-3022
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We assessed the prevalence and risk factors for irresistible daytime
sleepiness (IDS) in a cohort of patients with Parkinson's
disease (PD) treated with dopamine agonists. Seventy consecutive PD
patients on dopamine agonists were interviewed. IDS was experienced by 24
patients (34.3%). Fifty percent of the pramipexole patients, 15.4% of the
pergolide patients, 23.1% of the ropinirole patients and the 2
patients on bromocriptine experienced IDS. Patients who experienced IDS
were younger ($p = 0.009$). Nineteen patients had IDS while driving, 3
sustained a motor vehicle crash. Daytime somnolence ($p = 0.05$) and early
arousals ($p = 0.001$) were risk factors and daytime napping ($p = 0.007$) and
benzodiazepines ($p = 0.006$) were protective. Improvement was achieved by
changing the dosing schedule, the amount of agonist per dose, discontinuing
the agonist or accommodating the sleepiness. We conclude that dopamine
agonists are commonly implicated in IDS.
OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD
(5 CITINGS)
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 31 OF 331 MEDLINE on STN
ACCESSION NUMBER: 2002186257 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11917684
TITLE: [Treatment of Parkinson's syndrome].
Tretman Parkinsonovog sindroma.
AUTHOR: Zukic Tarik
CORPORATE SOURCE: Neuroloska klinika, Klinicki centar Univerzitata u
Sarajevu.
SOURCE: Medicinski arhiv, (2002) Vol. 56, No. 1, pp.
21-4.
Journal code: 0400722. ISSN: 0350-199X.
PUB. COUNTRY: Bosnia and Hercegovina
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Croatian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 3 Apr 2002
Last Updated on STN: 18 Apr 2002
Entered Medline: 17 Apr 2002
AB This paper discuss other possible approaches to the treatment od
Parkinson's disease and parkinsonism, particularly in
the case of younger patients. There is no doubt that levodopa treatment
has the major advance in the clinical management of parkinsonism
patients. However, the artificially of the levodopa decreases after

several years and motor complications appear. Precise diagnosis and estimated degree of disease are used before any treatment of parkinsonism. Anticholinergics or amantadine or dopamine agonists such as pergolide and bromocriptine are highly effective and they can delay the need for the levodopa.

L9 ANSWER 32 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 24

ACCESSION NUMBER: 2002:119525 BIOSIS
DOCUMENT NUMBER: PREV200200119525
TITLE: Pergolide protects SH-SY5Y cells against neurodegeneration induced by H2O2.
AUTHOR(S): Uberti, Daniela; Piccioni, Laura; Colzi, Anna; Bravi, Daniele; Canonico, Pier Luigi; Memo, Maurizio [Reprint author]
CORPORATE SOURCE: Department of Biomedical Sciences and Biotechnologies, School of Medicine, University of Brescia, Via Valsabbina 19, 25123, Brescia, Italy
memo@med.unibs.it
SOURCE: European Journal of Pharmacology, (2 January, 2002) Vol. 434, No. 1-2, pp. 17-20. print.
CODEN: EJPHAZ. ISSN: 0014-2999.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 2002
Last Updated on STN: 26 Feb 2002

AB We found that pergolide, a dopamine D1/D2 receptor agonist used in the clinical therapy of Parkinson's disease, protects SH-SY5Y neuroblastoma cells from cell death induced by a brief pulse (15 min) of 1 mM H2O2. Neuroprotection was found when pergolide was added to the culture medium either simultaneously with (EC50=60 nM) or 2 h before (EC50=40 nM) H2O2 treatment. These effects were not blocked by different dopamine receptor antagonists. Our data suggest that pergolide, independently of dopamine receptor stimulation, may interfere with the early phases of the oxidative stress-induced neurotoxic process.

L9 ANSWER 33 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 25

ACCESSION NUMBER: 2002:217033 BIOSIS
DOCUMENT NUMBER: PREV200200217033
TITLE: Pergolide in the treatment of patients with early and advanced Parkinson's disease.
AUTHOR(S): Bonuccelli, Ubaldo [Reprint author]; Colzi, Anna; Del Dotto, Paolo
CORPORATE SOURCE: Department of Neuroscience, University of Pisa, Via Roma, 67, 56126, Pisa, Italy
u.bonuccelli@neuro.med.unipi.it
SOURCE: Clinical Neuropharmacology, (January-February, 2002) Vol. 25, No. 1, pp. 1-10. print.
CODEN: CLNEDB. ISSN: 0362-5664.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Mar 2002
Last Updated on STN: 27 Mar 2002

AB Introduced on the market in 1989, pergolide, a D1/D2 dopamine receptor agonist, is still widely prescribed for the treatment of patients with early and advanced Parkinson's disease (PD). Initially, pergolide was introduced as an adjunct therapy to levodopa treatment in patients exhibiting fluctuating motor responses and dyskinesias. Results of recent randomized controlled clinical trials in de novo patients with PD show that pergolide is able to improve

parkinsonian symptoms when used as monotherapy. Moreover, preliminary results of a long-term monotherapy study in early PD suggest that pergolide is as effective as levodopa, and that a significant delay in the time of the onset of levodopa-induced motor complications can be obtained. A number of randomized studies have shown that pergolide is more effective than bromocriptine as adjunct therapy to levodopa in patients with advanced PD; the greater benefit found with pergolide could be ascribed to its action on both D1 and D2 dopamine receptors. However, controlled comparative studies with new dopamine agonists, such as ropinirole, cabergoline, and pramipexole, have not been performed yet. Interestingly, few open studies in patients with complicated PD have shown that high doses of pergolide (> 6 mg/d) are able to improve motor fluctuations and dyskinesias through a dramatic reduction of levodopa dosage. The side-effect profile of pergolide is similar to that of other dopamine agonists, and complications such as sleep attack and serosal fibrosis have been rarely reported.

L9 ANSWER 34 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 26

ACCESSION NUMBER: 2003:380949 BIOSIS
DOCUMENT NUMBER: PREV200300380949
TITLE: DOPAMINE AGONISTS SUPPRESS CHOLINOMIMETIC - INDUCED
TREMULOUS JAW MOVEMENTS IN AN ANIMAL MODEL OF PARKINSONISM:
EFFECTS OF CY 208 - 243, ROPINIROLE AND PERGOLIDE.
AUTHOR(S): Carlson, B. B. [Reprint Author]; Salamone, J. D.; Rios, C.;
Lentini, E.; Correa, M.; Wisniecki, A.; Betz, A.
CORPORATE SOURCE: Neurology, UCLA, School of Medicine, Los Angeles, CA, USA
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary
Planner, (2002) Vol. 2002, pp. Abstract No.
885.9. <http://sfn.scholarone.com.cd-rom>.
Meeting Info.: 32nd Annual Meeting of the Society for
Neuroscience. Orlando, Florida, USA. November 02-07, 2002.
Society for Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Aug 2003
Last Updated on STN: 20 Aug 2003

AB Considerable evidence indicates that cholinomimetic-induced tremulous jaw movements in rats share many characteristics with parkinsonian tremor. Tremulous jaw movements are defined as rapid vertical deflections of the lower jaw (3-7 Hz), which resemble chewing but are not directed at a particular stimulus. Several antiparkinsonian drugs suppress cholinomimetic-induced tremulous jaw movements. The present study investigated three different types of dopamine (DA) agonists, which have known antiparkinsonian characteristics, for their ability to suppress pilocarpine-induced tremulous jaw movements (4.0 mg/kg). The antiparkinsonian drug pergolide, which is a non-selective DA agonist, was highly potent at suppressing pilocarpine-induced jaw movements. The selective D2 agonist ropinirole, which also is used clinically as an antiparkinsonian drug, suppressed jaw movements in the dose range of 10.0-20.0 mg/kg. The selective D1 agonist CY 208-243, which suppresses tremor and has mild antiparkinsonian effects in humans, also reduced jaw movement activity (2.0-4.0 mg/kg). Across several studies, the rank order of potency for suppressing tremulous jaw movements in rats is related to the potency for producing antiparkinsonian effects in humans. Studies of cholinomimetic-induced jaw movements in rats can be used to characterize potential antiparkinsonian agents and to investigate the basal ganglia circuits involved in the generation of

tremulous movements.

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ACCESSION NUMBER: 2003:326914 BIOSIS
DOCUMENT NUMBER: PREV200300326914
TITLE: DISCRIMINATIVE STIMULUS (DS) PROPERTIES OF THE HIGHLY
SELECTIVE DOPAMINE D3/D2 RECEPTOR AGONIST, S32504.
AUTHOR(S): Dekeyne, A. [Reprint Author]; Iob, L. [Reprint Author];
Gobert, A. [Reprint Author]; Peglion, J. L. [Reprint
Author]; Millan, M. J. [Reprint Author]
CORPORATE SOURCE: Dept. Psychopharmacology, I.d.R. SERVIER,
Croissy-sur-Seine, France
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary
Planner, (2002) Vol. 2002, pp. Abstract No.
782.15. <http://sfn.scholarone.com>. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for
Neuroscience. Orlando, Florida, USA. November 02-07, 2002.
Society for Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jul 2003
Last Updated on STN: 22 Aug 2003

AB S32504 is a preferential agonist at D3 vs D2 receptors which shows low
affinity at all other sites (2). In a two-lever, food-reinforced, FR10
paradigm (1), rats were trained to recognise S32504 at a dose (0.04 mg/kg,
s.c.) which selectively decreased dialysis levels of dopamine vs serotonin
and norepinephrine in frontal cortex. As compared to its less potent
isomer, S32601, S32504 showed stereospecific generalization. Agents which
interact selectively with D3/D2 receptors vs serotonin receptors,
including piribedil, pramipexole, ropinirole, quinelorane and PD128,907,
generalized to S32504 with potencies correlating with those for induction
of other dopaminergic effects. In contrast, the D4 agonist, PD168,077,
and the D1/D5 agonist, SKF81297, failed to generalize. Potent blockade
was obtained with the D2 antagonists, L741,626 and S23199, and the D2/D3
antagonists, haloperidol, raclopride, AJ76 and UH232. Conversely, the D3
antagonists, GR218,231 and S33084, the D4 antagonist, S18126, and the
D1/D5 antagonist, SCH23390, were ineffective. Apomorphine, bromocriptine,
terguride, pergolide, cabergoline and lisuride weakly
generalized due to interference by their potent agonist properties at
serotonergic (5-HT_{2A/2C}) receptors. In conclusion, DS properties of
S32504 are mediated by D2 receptors. They are shared by other D3/D2
receptor agonists such as piribedil. However, they differ to
antiparkinsonian agents which also stimulate 5-HT_{2A/2C} receptors,
thereby "altering" mood. (1) Millan MJ et al, Neuropharmacology (2000)
39:586-598. (2) Millan MJ et al, Society Neurosci. Abstract

L9 ANSWER 36 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
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ACCESSION NUMBER: 2003:305601 BIOSIS
DOCUMENT NUMBER: PREV200300305601
TITLE: DIFFERENTIAL EFFICACY OF ANTIPARKINSONIAN (AP) AGENTS AT
DOPAMINE D2L RECEPTORS SUGGESTED BY G PROTEIN BUT NOT MAP -
KINASE ACTIVATION.
AUTHOR(S): Cussac, D. [Reprint Author]; Amphoux, A. [Reprint Author];
Hubert, D. [Reprint Author]; Newman-Tancredi, A. [Reprint
Author]; Millan, M. J. [Reprint Author]
CORPORATE SOURCE: Psychopharmacology, Inst de Rech Servier,
Croissy-sur-Seine, France
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary

Planner, (2002) Vol. 2002, pp. Abstract No.
542.1. <http://sfn.scholarone.com>. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for
Neuroscience. Orlando, Florida, USA. November 02-07, 2002.
Society for Neuroscience.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 2 Jul 2003

Last Updated on STN: 22 Aug 2003

AB D2 agonist-induced locomotor stimulation is mediated by post-synaptic striatal D2L receptors (2). Further, in a rat model of Parkinsons disease (unilateral lesion of substantia nigra), D2 agonists induced mitogen-activated protein kinase phosphorylation (MAPK-P)(1). Thus, we investigated G protein activation ((35S)GTPgammaS binding) and MAPK-P (immunodetection) in CHO-hD2L cells. Dopamine (DA)-stimulated G protein and MAPK-P were abolished by pertussis toxin implicating Gi/Go proteins. The D2 antagonists, L741,626 and raclopride, abolished DA-induced G protein activation and MAPK-P. Efficacies (Emax relative to DA=100%) for G protein activation/MAPK-P were as follows: roxindole (0%/92%), terguride (12/93), lisuride (21/105), piribedil (22/94), bromocriptine (28/92), S32504 (50/99), ropinirole (51/97), pergolide (52/103), apomorphine (53/91), pramipexole (70/95), cabergoline (70/105), talipexole (71/98), quinpirole (74/95) and quinlorane (102/102). Thus, whereas differential agonist properties of AP agents were seen for G-protein activation, all behaved as full agonists for MAPK-P. These data suggest substantial signal amplification between G proteins and downstream MAPK. Hence, "sub-maximal" efficacy at D2L receptor-coupled G proteins for drugs such as piribedil is sufficient for "full" AP actions. Further, "sub-maximal" efficacy may be preferential since it increases the therapeutic index between beneficial effects exerted in the striatum and side-effects elicited elsewhere. (1) Cai G. et al, J. Neurosci. (2000) 20:1849-1857.) (2) Usiello A. et al, Nature (2000) 408:199-203.

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ACCESSION NUMBER: 2003:282747 BIOSIS

DOCUMENT NUMBER: PREV200300282747

TITLE: DOPAMINE RECEPTOR AGONISTS USED FOR THE TREATMENT OF PARKINSON'S DISEASE DIFFERENTIALLY INFLUENCE HERG POTASSIUM CHANNEL FUNCTION AND CARDIAC ACTION POTENTIAL DURATION.

AUTHOR(S): Rutherford-Root, K. L. [Reprint Author]; Lawson, J. A. [Reprint Author]; Clark, M. A. [Reprint Author]; Higdon, N. R. [Reprint Author]; McDonald, W. G. [Reprint Author]; Hass, J. V. [Reprint Author]; McGrath, J. P. [Reprint Author]; Meglasson, M. D. [Reprint Author]; Hurst, R. S. [Reprint Author]

CORPORATE SOURCE: Pharmacology, Analytical and Medicinal Chemistry, Biostatics, Structural, Pharmacia Corp., Kalamazoo, MI, USA

SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No.
194.4. <http://sfn.scholarone.com>. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience. Orlando, Florida, USA. November 02-07, 2002.
Society for Neuroscience.

DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 19 Jun 2003

Last Updated on STN: 1 Aug 2003

AB In addition to the hallmark neuronal degeneration and impairment of motor

function, Parkinson's disease (PD) is associated with disturbances of the autonomic nervous system. As with other disorders of autonomic function, PD may be associated with increased risk of cardiovascular dysfunction including prolongation of the electrocardiographic QT interval. Therefore, 3 dopamine receptor agonists developed for the treatment of PD were evaluated for potential cardiovascular liability. Pergolide, ropinirole, and sumanirole were evaluated for the ability to inhibit the cardiac potassium channel HERG and/or to modify duration of ventricular Purkinje fiber action potentials. Pergolide and ropinirole inhibited HERG-mediated currents with IC₅₀ values of 0.12 μ M and 1.2 μ M, respectively. When evaluated in an action potential duration (APD) assay, pergolide significantly shortened APD at 90% repolarization (APD₉₀), whereas ropinirole significantly prolonged APD₉₀. Sumanirole weakly inhibited HERG (approx 15% at 10 μ M) and did not modify APD₉₀ over the tested concentration range (0.65-65 μ M). These results provide evidence that dopamine receptor agonists developed for the treatment of PD differentially modulate HERG channel function and APD. In addition, these findings demonstrate that sumanirole has a better profile with respect to 2 in vitro biomarkers of QT interval prolongation compared to ropinirole and pergolide.

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ACCESSION NUMBER: 2002073250 EMBASE
 TITLE: Long-term studies of dopamine agonists.
 AUTHOR: Hubble, Jean P., Dr. (correspondence)
 CORPORATE SOURCE: 371 McCampbell Hall, 1581 Dodd Drive, Columbus, OH 43210, United States. Hubble.5@osu.edu
 SOURCE: Neurology, (26 Feb 2002) Vol. 58, No. 4 SUPPL. 1, pp. S42-S50.
 Refs: 28
 ISSN: 0028-3878 CODEN: NEURAI
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 008 Neurology and Neurosurgery
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 7 Mar 2002
 Last Updated on STN: 7 Mar 2002

AB Dopamine agonists have long been used as adjunctive therapy for the treatment of Parkinson's disease (PD). In more recent years these drugs have also been proved safe and effective as initial therapy in lieu of levodopa in the treatment of PD. Long-term levodopa therapy is associated with motor complications, including fluctuating response patterns and dyskinesia. By initially introducing a dopamine agonist as symptomatic drug therapy, it may be possible to postpone the use of levodopa and delay or prevent the development of motor complications. Recently, four clinical trials have explored this hypothesis by comparing the long-term response and side effects of levodopa with dopamine agonist therapy. The drugs studied have included ropinirole, pramipexole, cabergoline, and pergolide. In each of these projects, the occurrence of motor complications, such as wearing off and dyskinesia, was significantly less in the subjects assigned to initiation of therapy with a dopamine agonist. The addition of levodopa could be postponed by many months or even several years. Therefore, these long-term studies of dopamine agonists support the initiation of a dopamine agonist instead of levodopa in an effort to postpone levodopa-related motor complications. This therapeutic approach may be particularly appropriate in PD patients

with a long treatment horizon on the basis of age and general good health. The extension phase of the long-term study comparing pramipexole with levodopa is ongoing, and follow-up information may help to establish the value of this treatment strategy.

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ACCESSION NUMBER: 2002047228 ESBIOBASE
TITLE: Long-term studies of dopamine agonists
AUTHOR(S): Hubble, Jean P.
CORPORATE SOURCE: Hubble, Jean P. (371 McCampbell Hall, 1581 Dodd Drive,
Columbus, OH 43210 (US))
SOURCE: Neurology (26 Feb 2002) Volume 58, Number 4
SUPPL. 1, 28 refs.
CODEN: NEURAI ISSN: 0028-3878
COUNTRY OF PUBLICATION: United States of America
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Feb 2009
Last updated on STN: 1 Feb 2009

AN 2002047228 ESBIOBASE

AB Dopamine agonists have long been used as adjunctive therapy for the treatment of Parkinson's disease (PD). In more recent years these drugs have also been proved safe and effective as initial therapy in lieu of levodopa in the treatment of PD. Long-term levodopa therapy is associated with motor complications, including fluctuating response patterns and dyskinesia. By initially introducing a dopamine agonist as symptomatic drug therapy, it may be possible to postpone the use of levodopa and delay or prevent the development of motor complications. Recently, four clinical trials have explored this hypothesis by comparing the long-term response and side effects of levodopa with dopamine agonist therapy. The drugs studied have included ropinirole, pramipexole, cabergoline, and pergolide. In each of these projects, the occurrence of motor complications, such as wearing off and dyskinesia, was significantly less in the subjects assigned to initiation of therapy with a dopamine agonist. The addition of levodopa could be postponed by many months or even several years. Therefore, these long-term studies of dopamine agonists support the initiation of a dopamine agonist instead of levodopa in an effort to postpone levodopa-related motor complications. This therapeutic approach may be particularly appropriate in PD patients with a long treatment horizon on the basis of age and general good health. The extension phase of the long-term study comparing pramipexole with levodopa is ongoing, and follow-up information may help to establish the value of this treatment strategy.

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STN DUPLICATE 27

ACCESSION NUMBER: 2002:69174 BIOSIS
DOCUMENT NUMBER: PREV200200069174
TITLE: Dopamine interacts directly with its D3 and D2 receptors on normal human T cells, and activates betal integrin function.
AUTHOR(S): Levite, M. [Reprint author]; Chowers, Y.; Ganor, Y.; Besser, M.; Herschkovits, R.; Cahalon, L.
CORPORATE SOURCE: Department of Human Microbiology, The Sackler School of Medicine, Tel Aviv University, Ramat Aviv, Tel Aviv, 69978, Israel
mia.levite@weizmann.ac.il
SOURCE: European Journal of Immunology, (December, 2001)
Vol. 31, No. 12, pp. 3504-3512. print.

CODEN: EJIMAF. ISSN: 0014-2980.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 16 Jan 2002

Last Updated on STN: 25 Feb 2002

AB Dopamine by itself has not up to now been reported to activate T cell function. We show here that dopamine interacts directly with dopaminergic receptors on normal human T cells and triggers betal integrin-mediated T cell adhesion to a major extracellular matrix component, fibronectin (FN). Such adhesion is a characteristic feature of activated T cells, and is critical for trafficking and extravasation of T cells across blood vessels and tissue barriers. Seven dopamine D2/D3 receptor agonists and antagonists were used to identify the receptor sub-types with which dopamine specifically interacts to activate T cells. The D3 dopamine receptor agonist, 7-hydroxy-DPAT (DPAT), mimics the effects of dopamine, and the effects of both dopamine and DPAT are blocked by a specific D3 receptor antagonist. U-maleate. The dopamine receptor agonists bromocriptine and pergolide mimic the direct effect of dopamine on the betal integrin function, while the dopamine receptor antagonists butaclamol and haloperidol suppress it, suggesting additional signaling via the dopamine D2 receptor sub-type. Our study shows, for the first time, that dopamine can directly activate T cells via its specific receptors and suggests a possible role for dopamine in integrin-mediated cellular trafficking and extravasation of T cells in the central nervous system and possibly also in the periphery. Finally, we suggest that the reported changes in the D3 and D2 receptor RNA levels in peripheral blood lymphocytes of individuals with schizophrenia, Parkinson's disease, Alzheimer's disease and migraine can serve not only as a 'passive' diagnostic marker, but primarily reflect the dynamic functional dopamine-T cell interactions in these diseases.

L9 ANSWER 41 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 28

ACCESSION NUMBER: 2001:361716 CAPLUS

DOCUMENT NUMBER: 135:90968

TITLE: Neostriatal muscarinic receptor subtypes involved in the generation of tremulous jaw movements in rodents. Implications for cholinergic involvement in Parkinsonism

AUTHOR(S): Salamone, John D.; Correa, Merce; Carlson, Brian B.; Wisniecki, Anna; Mayorga, Arthur J.; Nisenbaum, Eric; Nisenbaum, Laura; Felder, Christian

CORPORATE SOURCE: Dept. of Psychology, University of Connecticut, Storrs, CT, 06269-1020, USA

SOURCE: Life Sciences (2001), 68(22/23), 2579-2584

CODEN: LIFSAK; ISSN: 0024-3205

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Several studies have shown that a number of pharmacol. and neurochem. conditions in rats can induce jaw movements that are described as "vacuous" or "tremulous". For several years, there has been some debate about the clin. significance of various drug-induced oral motor syndromes. Nevertheless, considerable evidence now indicates that the non-directed, chewing-like movements induced by cholinomimetics have many of the characteristics of parkinsonian tremor. These movements are characterized largely by vertical deflections of the jaw, which occur in the same 3-7 Hz peak frequency that is typical of parkinsonian tremor. Cholinomimetic-induced tremulous jaw movements are suppressed by a number of different antiparkinsonian drugs, including scopolamine, benztropine, L-DOPA, apomorphine, bromocriptine, ropinirole, pergolide, amantadine, diphenhydramine and clozapine. A combination of anatomical and pharmacol. research in rats has implicated

M4 receptors in the ventrolateral neostriatum in the generation of tremulous jaw movements. Mice also show cholinomimetic-induced jaw movements, and M4 receptor knockout mice demonstrate substantially reduced levels of jaw movement activity, as well as increased locomotion. Taken together, these data are consistent with the hypothesis that a centrally-acting M4 antagonist may be useful as a treatment for parkinsonian symptoms, including tremor.

OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS
RECORD (16 CITINGS)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

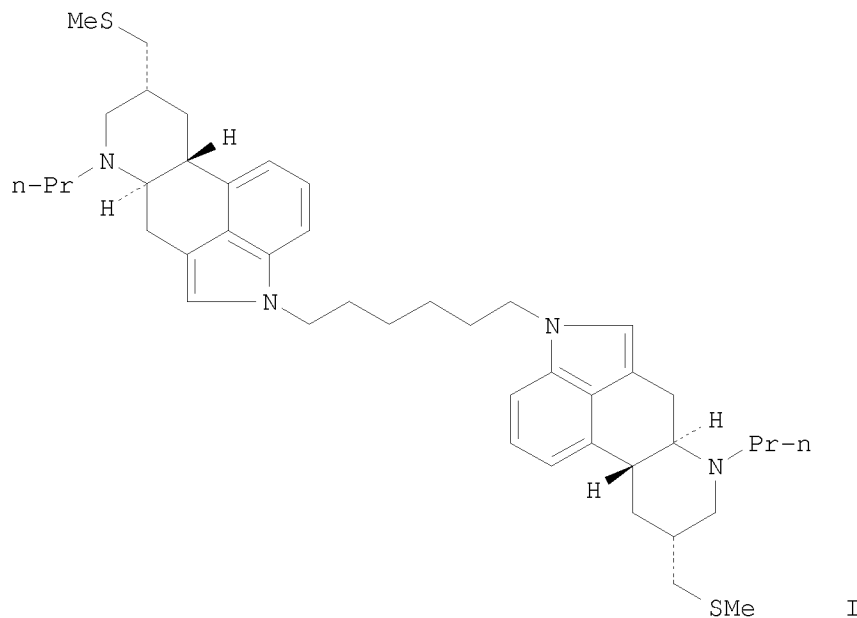
L9 ANSWER 42 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 29

ACCESSION NUMBER: 2001436469 EMBASE
TITLE: A 64-year-old man with parkinsonism as an initial symptom followed by dementia associated with marked abnormal behaviours.
AUTHOR: Suzuki, A.; Ikebe, S.-I.; Komatsuzaki, Y.; Takanashi, M.; Mori, H.; Hattori, N.; Mizuno, Y., Dr. (correspondence)
CORPORATE SOURCE: Department of Neurology, Juntendo Univ. School of Medicine, 2-1-1 Hongo, Bunkyo, Tokyo 113-8421, Japan. y_mizuno@med.juntendo.ac.jp
SOURCE: Brain and Nerve, (2001) Vol. 53, No. 11, pp. 1075-1087.
Refs: 33
ISSN: 0006-8969 CODEN: NOTOA6
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
ENTRY DATE: Entered STN: 3 Jan 2002
Last Updated on STN: 3 Jan 2002

AB We report a 64-year-old man with parkinsonism as an initial symptom, which was followed by dementia and abnormal behaviours. He was well until 1985, when he was 49 years old, when he noted rest tremor in his right hand. Soon tremor appeared in his left hand as well. He was seen in our clinic and levodopa was prescribed. He was doing well with this medication, however, in 1993, he started to suffer from on-off phenomenon. He also noted visual hallucination. In 1994, he stole a watermelon and ate it in the shop. He repeated such abnormal behaviours. In 1995, he was admitted to the neurology service of Hatsuishi Hospital. On admission, he was alert and oriented. He did not seem to be demented; however, he admitted stealing and hypersexual behaviours. No aphasia, apraxia, or agnosia was noted. In the cranial nerves, downward gaze was markedly restricted. He showed masked and seborrheic face, and small voice. No motor palsy was noted, but he walked in small steps with freezing and start hesitation. Marked neck and axial rigidity was noted. Tremor was absent except for in the tongue. No cerebellar ataxia was noted. Deep tendon reflexes were diminished. Plantar response was extensor bilaterally. Forced grasp was noted also bilaterally. He was treated with levodopa and pergolide, but he continued to show on-off phenomenon. His balance problem and akinesia became progressively worse; still he showed hypersexual behaviour problems. He also showed progressive decline in cognitive functions. In 1997, he started to show dysphagia. He developed aspiration pneumonia in July of 1998. In 1999, he developed emotional incontinence and became unable to walk. He also developed repeated aspiration pneumonia. He died on March 1, 2000. He was discussed in a neurological CPC and the chief discussant arrived at a conclusion that the patient had corticobasal degeneration. Other

diagnoses entertained included dementia with Lewy bodies, diffuse Lewy body disease, and frontotemporal dementia. Majority of the participants thought that diffuse Lewy body disease was most likely. Post-mortem examination revealed marked nigral neuronal loss, gliosis and Lewy bodies in the remaining neurons. Abundant Lewy bodies of cortical type were seen wide spread in the cortical areas, but particularly many in the amygdaloid nucleus. Lewy bodies were also seen in the subcortical structures such as the dorsal motor nucleus, oculomotor nucleus, Meynert nucleus, putamen, and thalamus. What was interesting was marked neuronal loss of the pontine nuclei, demyelination of the pontocerebellar fiber, and moderate neuronal loss of the cerebellar Purkinje neurons, a reminiscent of pontocerebellar atrophy. However, the inferior olivary nucleus was intact.

L9 ANSWER 43 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 30
 ACCESSION NUMBER: 2001:430539 CAPLUS
 DOCUMENT NUMBER: 135:166952
 TITLE: Semisynthetic dimers of antiparkinsonic ergot alkaloids
 AUTHOR(S): Kren, Vladimir; Weignerova, Lenka; Kuzma, Marek; Jegorov, Alexandr; Sedmera, Petr
 CORPORATE SOURCE: Institute of Microbiology, Academy of Sciences of the Czech Republic, Prague, CZ 142 20/4, Czech Rep.
 SOURCE: Heterocycles (2001), 55(6), 1045-1056
 CODEN: HTCYAM; ISSN: 0385-5414
 PUBLISHER: Japan Institute of Heterocyclic Chemistry
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 135:166952
 GI



AB 1,1-Linked dimers, e.g. I, of semisynthetic ergoline alkaloids with antiparkinsonic activity were prepared in 60 - 63% yield from the parent compds. (pergolide, terguride) by action of

α,ω -dihalogenalkanes in DMSO/KOH. N-1- ω -Halogenalkyl pergolide and terguride precursors were used for the synthesis of non-sym. dimers. N-6 Alkylation was achieved (yield 18 - 28%) using 1,6-dihalogenohexane in DMF/K₂CO₃.

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 44 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 31
ACCESSION NUMBER: 2001:679198 CAPLUS
DOCUMENT NUMBER: 135:366649
TITLE: Cost-effectiveness analysis of dopamine agonists in the treatment of Parkinson's disease in Japan
AUTHOR(S): Shimbo, Takuro; Hira, Kenji; Takemura, Manabu; Fukui, Tsuguya
CORPORATE SOURCE: Department of General Medicine and Clinical Epidemiology, Graduate School of Medicine, Kyoto University, Kyoto, Japan
SOURCE: PharmacoEconomics (2001), 19(8), 875-886
CODEN: PARMEK; ISSN: 1170-7690
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dopamine agonists such as bromocriptine or pergolide are often used in Japan to treat Parkinson's disease. Dopamine agonists are relatively expensive drugs; economic evaluations are required. Aim of this study was to evaluate the cost effectiveness of dopamine agonists for the treatment of Parkinson's disease in Japan. We used a Markov model to simulate the course of Parkinson's disease and to compare the cost effectiveness of dopamine agonists added to levodopa with that of levodopa alone in Japan. The model assumed that 60-yr-old men with Parkinson's disease in Hoehn-Yahr (HY) stages 2 to 5 using levodopa were administered dopamine agonists or continued on levodopa alone. The incremental cost effectiveness of dopamine agonists used for 10 yr was then estimated. In the patients in HY stage 2, the incremental cost effectiveness of dopamine agonists was 18 610 000 to 19 320 000 yen () per quality-adjusted life-year (QALY) [\$US172 300 to \$US178 900/QALY; 1998 values]. In patients in HY stage 3 or higher, the use of dopamine agonists was dominant over levodopa alone mainly due to reduced cost for care. In sensitivity analyses, costs and effectiveness of dopamine agonists significantly influenced the results. The use of a generic formulation of bromocriptine was dominant over levodopa alone even in the patients with HY stage 2 disease. Dopamine agonists appear to be cost effective in advanced Parkinson's disease, although their use is sensitive to the costs and effectiveness of dopamine agonists. If factors discouraging the prescription of generic drugs in Japan were removed, the treatment of Parkinson's disease would become more cost effective.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 45 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 32
ACCESSION NUMBER: 2003014257 EMBASE
TITLE: Randomized trial of tolcapone versus pergolide as add-on to levodopa therapy in Parkinson's disease patients with motor fluctuations.
AUTHOR: Koller, William
CORPORATE SOURCE: University of Miami, Department of Neurology, 1501 NW 9th

Avenue, Miami, FL 33136, United States.

AUTHOR: Lees, Andrew; Doder, Miroslava
CORPORATE SOURCE: Natl. Hosp. for Neurol./Neurosurgery, London, United Kingdom.

AUTHOR: Hely, Mariese
CORPORATE SOURCE: Westmead Hospital, Sydney, Australia.

AUTHOR: Burns, R.
CORPORATE SOURCE: Finders Medical Center, Adelaide, SA, Australia.

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CORPORATE SOURCE: Austin and Repatriation Med. Center, Heidelberg, United Kingdom.

AUTHOR: Morris, J.
CORPORATE SOURCE: Westmead General Hospital, Westmead, United Kingdom.

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CORPORATE SOURCE: Weston General Hospital, Weston Super Mare, Avon, United Kingdom.

AUTHOR: Capildeo, R.
CORPORATE SOURCE: Orsett Hospital, Orsett, Grays, Essex, United Kingdom.

AUTHOR: Clark, C.E.
CORPORATE SOURCE: Hull Royal Infirmary, Hull, United Kingdom.

AUTHOR: Forsyth, D.R.
CORPORATE SOURCE: Addenbrookes NHS Trust, Cambridge, United Kingdom.

AUTHOR: Lees, A.J.
CORPORATE SOURCE: Natl. Hosp. for Neurology/Neurosurg., London, United Kingdom.

AUTHOR: Mondal, B.K.
CORPORATE SOURCE: Rotherham District General Hospital, Oakwood, Rotherham, United Kingdom.

AUTHOR: Sharma, J.C.
CORPORATE SOURCE: Community Hospital, Nottingham, United Kingdom.

AUTHOR: Steiger, M.J.
CORPORATE SOURCE: Walton Centre for Neurol./Neurosurg., Liverpool, United Kingdom.

AUTHOR: Comella, C.L.
CORPORATE SOURCE: Rush-Presbyterian St Lukes Med. Ctr., Chicago, IL, United States.

AUTHOR: Davis, T.L.
CORPORATE SOURCE: Vanderbilt University, Nashville, TN, United States.

AUTHOR: Hauser, R.A.
CORPORATE SOURCE: Tampa General Hospital, Tampa, FL, United States.

AUTHOR: Hutton, J.T.
CORPORATE SOURCE: St Mary of the Plains Hospital, Lubbock, TX, United States.

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CORPORATE SOURCE: University of Kansas Medical Center, Kansas City, KS, United States.

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CORPORATE SOURCE: Barrow's Neurological Institute, Phoenix, AZ, United States

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CORPORATE SOURCE: Mount Sinai Hospital, Cleveland, OH, United Kingdom.

AUTHOR: Roduitzky, R.L.
CORPORATE SOURCE: University of Iowa Hospitals, Iowa City, IA, United States.

AUTHOR: Saint-Hilaire, M.-H.
CORPORATE SOURCE: Boston University School of Medicine, Boston, MA, United States.

AUTHOR: Waters, C.H.
CORPORATE SOURCE: University of Southern California, Los Angeles, CA, United States.

AUTHOR: Watts, R.L.
CORPORATE SOURCE: The Emory Clinic, Atlanta, GA, United States.
AUTHOR: Koller, W.C., Dr. (correspondence)
CORPORATE SOURCE: Department of Neurology, University of Miami Medical Center, 1501 NW 9th Avenue, Miami, FL 33136, United States.
SOURCE: Movement Disorders, (Sep 2001) Vol. 16, No. 5, pp. 858-866.
Refs: 27
ISSN: 0885-3185 CODEN: MOVDEA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 020 Gerontology and Geriatrics
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
006 Internal Medicine
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jan 2003
Last Updated on STN: 16 Jan 2003

AB In this 12-week, randomized, open-label, blinded-rater, parallel-group trial, the efficacy, safety, and tolerability of tolcapone and pergolide were compared in parkinsonian patients with a fluctuating response to levodopa. Patients received tolcapone 100 mg three times daily (t.i.d.), with a possible increase to 200 mg t.i.d., or pergolide titrated to a maximum dose of 5 mg/day by week 9 (mean final dose 2.2 mg/day). The trial involved 203 patients. Efficacy variables that decreased from baseline to week 12 with tolcapone and pergolide included "off" time (reduced by 2-3 hours/day), daily levodopa intake, sickness impact profile scores, Parkinson's disease questionnaire (PDQ)-39 scores, and Unified Parkinson's Disease Rating Scale (UPDRS) scores. Improvements in efficacy variables were similar with tolcapone and pergolide, with the exception of improvements in quality of life, which were significantly greater with tolcapone; the relative changes in PDQ-39 score at week 12 were -8.7 and -14.2 ($P < 0.05$) with pergolide and tolcapone, respectively. Improvements in the investigator's global assessment (IGA) of overall efficacy were recorded in 86% of tolcapone-treated patients and in 78% of pergolide-treated patients. The proportion of patients who withdrew because of adverse events was higher in the pergolide group (15%) than in the tolcapone group (5%). Confusion, hypotension, nausea, constipation, abdominal pain, and dyspepsia occurred more frequently with pergolide, whereas diarrhea and urine discoloration occurred more frequently with tolcapone. Tolcapone was better tolerated than pergolide ($P < 0.01$) according to the IGA of overall tolerability. We conclude that, in this 3-month study, both tolcapone and pergolide provided improvements in motor fluctuations and allowed reductions in levodopa intake when added to levodopa therapy; intent to treat analysis and a less than maximal dose of pergolide may have biased the results in favor of tolcapone. Tolcapone provided greater improvements in quality of life, was better tolerated, and had a more favorable adverse-event profile than pergolide. .COPYRG. 2001 Movement Disorder Society.

L9 ANSWER 46 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:499785 BIOSIS
DOCUMENT NUMBER: PREV200100499785
TITLE: SLV308: Antiparkinsonian effects in the MPTP-treated common marmoset (*Callithrix jacchus*).
AUTHOR(S): Johnston, L. C. [Reprint author]; Smith, L. [Reprint

author]; McCreary, A. C.; Jenner, P. [Reprint author]; Ronken, E.

CORPORATE SOURCE: Neurodegenerative Diseases Research Centre, Division of Pharmacology and Therapeutics, Kings College London, London, SE1 1UL, UK

SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 531. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience. San Diego, California, USA. November 10-15, 2001.
ISSN: 0190-5295.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 24 Oct 2001
Last Updated on STN: 23 Feb 2002

AB SLV308 is a novel non-ergot compound combining partial agonism at the dopamine D2 receptor with full agonism at the 5-HT1A receptor. As such, SLV308 is likely to be a clinically relevant anti-parkinsonian agent with a broader range of therapeutic effects (cf. McCreary et al., this meeting; Feenstra et al., 2001; Drugs of the Future, in press). Hence, SLV308 has been examined in the MPTP-treated common marmoset, an animal model which has very good predictive validity for testing anti-parkinsonian drugs. Domperidone was given 40 minutes prior to intraperitoneal (ip) or oral (po) administration of SLV308 (0.01-0.3 mg/kg) in separate experiments. A modified latin-square design was employed with 7 days between treatments and the experimenter blind to the treatment groups. SLV308 (0.3 mg/kg) induced a 663% (ip) and 855% (po) increase in total locomotor counts compared to the vehicle group (11 and 8 hours after administration, respectively, $p < 0.05$). The corresponding least effective doses (LEDs) were 0.03 mg/kg ip and 0.03 mg/kg po. This was associated with a corresponding 65% and 53% decrease in total motor disability scores, respectively. The LEDs for the reversal of disability scores were 0.01 mg/kg (ip) and 0.03 mg/kg (po). Thus, SLV308 has high potency in the MPTP-treated marmoset and since similar qualitative results are seen with other known anti-parkinsonian agents such as ropinirole, pergolide, talipexole and L-DOPA it is expected to be effective for the treatment of Parkinson's disease.

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ACCESSION NUMBER: 2001:497486 BIOSIS

DOCUMENT NUMBER: PREV200100497486

TITLE: Evaluation of different neuroprotective strategies in a retrograde nigrostriatal lesion model of Parkinson's disease in the rat.

AUTHOR(S): O'Neill, M. J. [Reprint author]; Murray, T. K. [Reprint author]; Swettenham, J. B. [Reprint author]; Hicks, C. A. [Reprint author]; Ward, M. A. [Reprint author]; Dobson, D. R. [Reprint author]

CORPORATE SOURCE: Dept Histopathol, Eli Lilly and Co, Surrey, UK

SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 528. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience. San Diego, California, USA. November 10-15, 2001.
ISSN: 0190-5295.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 24 Oct 2001
Last Updated on STN: 23 Feb 2002

AB Current treatment strategies for Parkinson's disease (PD) are only symptomatic, an ideal drug would slow or halt progression of the disease. We have evaluated drugs with various mechanisms of action that may provide a neuroprotective action in PD. We have examined the effect of SIB-1553A (neuronal nicotinic agonist), pergolide (dopamine agonist), LY379268 (mGluR2/3 agonist) and KF17837 (adenosine A2A antagonist) in a striatal 6-OHDA model of PD in the rat. 6OHDA (10µg) was infused stereotaxically into the right striatum of male Sprague Dawley rats (280-320g). In 2 experiments animals were treated with SIB1553A (20 mg/kg s.c.), pergolide (1 mg/kg i.p.), LY379268 (10 mg/kg i.p.), KF17837 (10 mg/kg p.o.) or vehicle for 28 days, beginning 1 day after 6-OHDA infusion. Rats were perfused transcardially with formalin at 28 days and the brains removed for histological analysis. Tyrosine hydroxylase immunohistochemistry (TH-I) was used to assess dopaminergic neuronal degeneration in the striatum and substantia nigra. Results indicated that 10 µg of 6-OHDA produced a 40-50% loss of nigra cells at 28 days after infusion. SIB1553A and LY379268 provided significant protection ($p < 0.05$), while in contrast pergolide and KF17837 had no effect. These results suggest that although D2 agonists and A2A antagonists provide symptomatic improvement in PD they appear to have no effect on disease progression. In contrast, both nicotinic agonists and group II mGluR agonists can neuroprotect in this model and may provide new targets to prevent neurodegeneration in PD.

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STN DUPLICATE 33

ACCESSION NUMBER: 2001:330797 BIOSIS

DOCUMENT NUMBER: PREV200100330797

TITLE: Pharmacological effects of cabergoline against parkinsonism.

AUTHOR(S): Ichikawa, Kiyoshi [Reprint author]; Kojima, Masami [Reprint author]

CORPORATE SOURCE: Pharmacology Research R and D, Kissei Pharmaceutical Co., Ltd., 4365-1 Kashiwabara, Hotaka, Minamiazumi, Nagano, 399-8304, Japan
kiyoshi_ichikawa@pharm.kissei.co.jp

SOURCE: Folia Pharmacologica Japonica, (June, 2001) Vol. 117, No. 6, pp. 395-400. print.
CODEN: NYKZAU. ISSN: 0015-5691.

DOCUMENT TYPE: Article

LANGUAGE: Japanese

ENTRY DATE: Entered STN: 11 Jul 2001

Last Updated on STN: 19 Feb 2002

AB The pharmacological effects of cabergoline, a novel ergot alkaloid, against parkinsonism were assessed by comparing its effects with those of bromocriptine and pergolide. The affinities of cabergoline and pergolide for the D2 receptor were about the same, about 7 times stronger than that of bromocriptine. The affinity of each compound for the D1 receptor was markedly lower than its affinity for the D2 receptor. However, other data suggest that cabergoline and pergolide would have D1-receptor agonist activity, whereas bromocriptine would act as a D1-receptor antagonist. In MPTP-lesioned parkinsonian monkeys, cabergoline improved motor disability, and its effect lasted longer than those of bromocriptine and pergolide. Moreover, cabergoline induced no behavioral abnormalities even though at the highest dose used, in contrast to bromocriptine and pergolide, both of which induced hyperactivity. This beneficial effect of cabergoline did not attenuate on prolonged administration. Combined treatment with a low dose of L-dopa and a low dose of cabergoline improved motor disability without inducing the hyperactivity and dyskinesia seen during treatment with L-dopa alone at high doses. From these results, we suggest that cabergoline promises to be a useful anti-

parkinsonian agent with a long lasting effect that survives
prolonged administration and without the side effects induced by L-dopa.

L9 ANSWER 49 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 34

ACCESSION NUMBER: 2001:487413 CAPLUS

DOCUMENT NUMBER: 136:226133

TITLE: Are dopamine receptor agonists neuroprotective in
Parkinson's disease?

AUTHOR(S): Le, Wei-Dong; Jankovic, Joseph

CORPORATE SOURCE: Department of Neurology, Baylor College of Medicine,
Houston, TX, USA

SOURCE: Drugs & Aging (2001), 18(6), 389-396

CODEN: DRAGE6; ISSN: 1170-229X

PUBLISHER: Adis International Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Dopamine receptor agonists are playing an increasingly important role in the treatment of not only patients with advanced Parkinson's disease and those with levodopa-induced motor fluctuations, but also in the early treatment of the disease. This shift has been largely due to the demonstrated levodopa-sparing effect of dopamine agonists and their putative neuroprotective effect, with evidence for the latter being based largely on exptl. in vitro and in vivo studies. In this article we review the evidence for neuroprotection by the dopamine agonists pramipexole, ropinirole, pergolide, bromocriptine and apomorphine in cell cultures and animal models of injury to the substantia nigra. Most of the studies suggest that dopamine agonists may have neuroprotective effects via direct scavenging of free radicals or increasing the activities of radical-scavenging enzymes, and enhancing neurotrophic activity. However, the finding that pramipexole can normalize mitochondrial membrane potential and inhibit activity of caspase-3 in cytoplasmic hybrid cells derived from mitochondrial DNA of patients with nonfamilial Alzheimer's disease suggests an even broader implication for the neuroprotective role of dopamine agonists. Although the clin. evidence for neuroprotection by dopamine agonists is still limited, the preliminary results from several ongoing clin. trials are promising. Several longitudinal studies are currently in progress designed to demonstrate a delay or slowing of progression of Parkinson's disease using various surrogate markers of neuronal degeneration such as 18F-levodopa positron emission tomog. and 123I β -CIT (carbomethoxy- β -4-iodophenyl-nortropane) single positron emission computed tomog. The results of these exptl. and clin. studies will improve our understanding of the action of dopamine agonists and provide critical information needed for planning future therapeutic strategies for Parkinson's disease and related neurodegenerative disorders.

OS.CITING REF COUNT: 44 THERE ARE 44 CAPLUS RECORDS THAT CITE THIS
RECORD (44 CITINGS)

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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STN DUPLICATE 35

ACCESSION NUMBER: 2001:406014 BIOSIS

DOCUMENT NUMBER: PREV200100406014

TITLE: Pleuropulmonary disease due to pergolide use for restless
legs syndrome.

AUTHOR(S): Danoff, Sonye K.; Grasso, Marc E.; Terry, Peter B.; Flynn,
John A. [Reprint author]

CORPORATE SOURCE: Johns Hopkins Outpatient Center, Johns Hopkins University,
601 North Caroline St, No. 7143, Baltimore, MD, 21287, USA

SOURCE: Chest, (July, 2001) Vol. 120, No. 1, pp. 313-316.

print.
CODEN: CHETBF. ISSN: 0012-3692.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Aug 2001
Last Updated on STN: 22 Feb 2002

AB Pergolide is an ergot-derived dopamine agonist used in Parkinson's disease and, increasingly, in restless legs syndrome. We report a patient with a 2.5-year history of weight loss, pleuropulmonary fibrosis, and exudative pleural effusion that developed insidiously while taking this medication. The extensive and invasive workup that preceded the diagnosis high-lights the difficulty in attributing such a process to a drug reaction. This is the second report of such a reaction to pergolide, which is one of the increasing number of ergot-derived compounds in common clinical use.

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ACCESSION NUMBER: 2001291374 EMBASE
TITLE: Cost-effectiveness of pergolide compared to bromocriptine in the treatment of Parkinson's disease: A decision-analytic model.
AUTHOR: Davey, P. (correspondence); Rajan, N.; Lees, M.; Aristides, M.
CORPORATE SOURCE: M-TAG Pty Ltd, PO Box 5639, Chatswood, NSW 1515, Australia. pdavey@m-tag.net
SOURCE: Value in Health, (2001) Vol. 4, No. 4, pp. 308-315.
Refs: 14
ISSN: 1098-3015 CODEN: VIHLFM
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Aug 2001
Last Updated on STN: 30 Aug 2001

AB Objective: To develop a decision-analytic model to assess the cost-effectiveness of pergolide versus bromocriptine in the treatment of Parkinson's disease (PD). Methods: A Markov decision-analytic model is used to examine cost-effectiveness. The model ran for 20 cycles of 6 months' duration, and the patients progress through six stages: Hoehn-Yahr stages 1-5 and death. The transitional probabilities for each stage are derived from a 12-year longitudinal study of patients with PD. The costs in the model are derived from an expert panel containing six Australian neurologists. A review of the randomized controlled trials comparing the efficacy and safety of pergolide versus bromocriptine was undertaken. Five studies were identified, with four showing that pergolide offers superior efficacy when compared to bromocriptine. The Mizuno et al. (1995) study was the largest of the controlled trials and also measured patient Hoehn-Yahr status before and after treatment. This was identified as the most appropriate source of relative efficacy data for the model. The model examined various scenarios based on alternate durations of superior clinical benefit with pergolide compared to bromocriptine. The main analysis assumed that patients in each arm of the model would have identical Hoehn-Yahr status by the fifth year. Sensitivity analysis was used to determine cost-effectiveness in the case where the therapeutic

benefit was of a shorter duration. Results: The Mizuno study indicates that an additional 19.09% of patients improved by at least one stage on pergolide over bromocriptine, with an odds ratio of 2.26 ($p < .01$). The total health care cost per patient over the 10-year period was \$46,323 in the pergolide treatment arm and \$47,351 in the bromocriptine treatment arm, an incremental saving of \$1028. Patients also spent extra time in Hoehn-Yahr stages 1, 2, and 3. In sensitivity analyses, when the benefit from pergolide expired between 6 months and 5 years after treatment cessation, cost savings ranged from \$68 to \$2535. Conclusion: Pergolide is cost saving and more efficacious than bromocriptine, and is therefore cost-effective.

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ACCESSION NUMBER: 2002036123 EMBASE

TITLE: [Switch from conventional selegiline to xilopar® allows dose reduction of levodopa and dopamine agonists].
Umstellung von konventionellen selegilin-präparaten auf xilopar® ermöglicht die reduktion von l-dopa und dopamin-agonisten.

AUTHOR: Holtmann, Wolfgang, Dr. (correspondence)

CORPORATE SOURCE: Arzt für Neurologie, Schlossplatz 6, 91207 Lauf, Germany.

SOURCE: Neurologie und Rehabilitation, (2001) Vol. 7, No. 6, pp. 298-300.

Refs: 4

ISSN: 0947-2177 CODEN: NEREF3

COUNTRY: Germany

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 037 Drug Literature Index

008 Neurology and Neurosurgery

LANGUAGE: German

SUMMARY LANGUAGE: English; German

ENTRY DATE: Entered STN: 7 Feb 2002

Last Updated on STN: 7 Feb 2002

AB The anti-parkinsonian drug selegiline has successfully been used for years in order to achieve a levodopa sparing effect. The need for levodopa therapy can be delayed by an average of 9 months. In addition, various placebo-controlled studies demonstrated that the levodopa dose can be maintained almost stable for a period of at least 5 years when used in combination with selegiline. On the other hand, therapy with conventional selegiline is limited, e. g. by the contra-indication in patients with impaired hepatic or renal function, the possible disturbance of night-time sleep by the amphetamine metabolites, and by the high variability in bioavailability because of an extensive first-pass effect. In Xilopar®, selegiline is presented as a lyophilised tablet that can circumvent these problems. In this case report, the switch from conventional selegiline to Xilopar® lead to a dose reduction of levodopa as well as pergolide associated with very good symptom control. Xilopar® was well tolerated and resulted in a considerable improvement of the patient's quality of life.

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ACCESSION NUMBER: 2001:305811 BIOSIS

DOCUMENT NUMBER: PREV200100305811

TITLE: Polysomnographic measures in Parkinson's disease: A comparison between patients with and without REM sleep disturbances.

AUTHOR(S): Wetter, Thomas C. [Reprint author]; Trenkwalder, Claudia; Gershanik, Oscar; Hoegl, Birgit

CORPORATE SOURCE: Max Planck Institute of Psychiatry, Kraepelinstrasse 10, D-80804, Munich, Germany

SOURCE: wetter@mpipsykl.mpg.de
Wiener Klinische Wochenschrift, (17 April, 2001)
Vol. 113, No. 7-8, pp. 249-253. print.
CODEN: WKWOAO. ISSN: 0043-5325.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 27 Jun 2001

Last Updated on STN: 19 Feb 2002

AB Study objective: To assess the frequency of rapid eye movement (REM) sleep abnormalities in Parkinson's disease (PD) patients and compare polygraphic sleep measures in those with and without REM sleep disturbances. Design: Polysomnographic recordings of 2 consecutive nights were performed in 45 patients with PD (mean age 65 years, mean Hoehn and Yahr stage 2.2). Twenty patients were treated with dopaminergic drugs, 10 were drug-free for two weeks and 15 had never been treated with L-dopa or dopamine agonists. According to the polysomnographic findings, the patients were divided into those with and without REM sleep abnormalities. Abnormal REM sleep features were defined as REM sleep without atonia (RWA) and REM sleep behavior disorder (RBD). Results: Eighteen (40%) of the PD patients showed either RWA (24%; 6 men, 5 women) or RBD (16%; 6 men, 1 woman). Patients with REM sleep disturbances had a significantly longer duration of the disease (8.3 vs. 3.9 years), a more severe stage of the disease (2.6 vs. 2.0 Hoehn and Yahr stage) and were treated with a higher dosage of dopaminergic drugs (L-dopa, pergolide and bromocriptin). 67% of the patients with normal REM sleep were untreated at the time of the sleep study, but only 39% of those with REM sleep abnormalities. Sleep EEG measures (sleep efficiency, sleep onset latency, sleep period time, relative amounts of sleep stages) for the second night showed no significant differences between both groups apart from a significantly lower sleep period time in PD patients with RWA/RBD. Conclusions: Abnormal REM sleep features are a frequent finding in patients with PD. The prevalence seems to increase with a longer disease duration. Therefore, a careful follow-up is necessary. A sleep architecture not different from PD patients without RWA/RBD suggests that the underlying abnormality is confined to REM sleep.

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ACCESSION NUMBER: 2001277697 EMBASE

TITLE: Pergolide mesylate (Permax®) as adjuvant treatment of Parkinson's disease-prospective, open 6-month study.

AUTHOR: Bares, M., Dr. (correspondence); Rektor, I.; Kanovsky, P.; Hortova, H.; Streitova, H.; Kubova, D.; Rektorova, I.

CORPORATE SOURCE: I. Neurologicka Klinika LF MU, FN U su. Anny, Pekarska 53, 656 91 Brno, Czech Republic. martin.bares@fnusa.cz

SOURCE: Ceska a Slovenska Neurologie a Neurochirurgie, (2001) Vol. 64, No. 4, pp. 231-236.

Refs: 24

ISSN: 1210-7859 CODEN: CKNNAS

COUNTRY: Czech Republic

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 037 Drug Literature Index

038 Adverse Reactions Titles

008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 23 Aug 2001

Last Updated on STN: 23 Aug 2001

AB Twenty-four patients with idiopathic Parkinson's disease were followed up perspectively during a 6-month period to test the incidence of undesirable effects of the preparation pergolide mesylate (Permax®). Pergolide was administered to patients as

adjuvant treatment to current medicamentous treatment with preparations containing L-DOPA. Before starting treatment in every patient the Unified Parkinson's Disease Rating Scale (UPDRS) was used, the stage of the disease was assessed according to Hoehn and Yahra, the scale of daily activities according to Schwab and England, blood pressure and heart rate were assessed in a recumbent and upright position. During subsequent visits the authors assessed the effectiveness of pergolide by means of the UPDRS score parts III, IV, the duration during the wakeful state spent in dyskinesias, duration of the "off" condition of mobility and the CGI score (Clinical Global Impression) was evaluated (weeks 2, 4, 8 and 16). During every visit the authors monitored blood pressure readings, pulse rate and undesirable effects of the preparation. During week 24 (end of the investigation) again the complete UPDRS scale was tested. The mean pergolide daily dose was 2.85 ± 0.45 mg. Reduction of the total daily dose of L-DOPA (from 906 mg to 664 mg levodopa per day) or reduction of other antiparkinsonian medication was effectuated during pergolide administration in particular during development or deterioration of dyskinesias. The most frequent undesirable effects were disorders of orthostasis (14.3 % patients), gastrointestinal complaints (9.5 %), insomnia (9.5 %), hypersexuality (9.5 %). In 21 patients (87.5 %) who finished the complete follow up no significant changes were observed in the values of blood pressure or heart rate. In three patients (12.5 %) pergolide had to be discontinued prematurely - in one because of visual hallucinations, in another two because of subjective symptoms of orthostatic hypotension and gastrointestinal complaints. The total UPDRS score (reduction by 48.3 %) as well as the UPDRS III score (Motor Examination - reduction by 56.2 %), UPDRS IV (Complications of Therapy - reduction by 40 %) and UPDRS II (Everyday Activities - reduction by 37.6 %) were significantly lower after 24 weeks of pergolide administration as compared with baseline values before treatment was started. The UPDRS I score (Thinking, Behaviour and Mood) was not significantly influenced at the end of the investigation period (reduction by 5.3 %). The time of wakefulness spent in an "off" state was reduced by 53.0 %, the duration of dyskinesias by 29.8 %. Pergolide mesylate (Permax®) is an effective and safe preparation suitable for adjuvant therapy with preparations containing levodopa in the treatment of idiopathic Parkinson's disease.

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ACCESSION NUMBER: 2001212834 EMBASE

TITLE: [Pharmacotherapy of idiopathic parkinson's syndrome with special focus on neuroprotection].
Pharmakotherapie des idiopathischen parkinson-syndroms unter besonderer berucksichtigung neuroprotektiver therapiestrategien.

AUTHOR: Reichmann, H., Dr. (correspondence); Sommer, U.; Gerlach, M.; Riederer, P.

CORPORATE SOURCE: Klinik und Poliklinik fur Neurologie, Univ. klinikum Carl Gustav Carus, Technische Universitat Dresden, Fetscherstrasse 74, D-01307 Dresden, Germany.

SOURCE: Nervenheilkunde, (2001) Vol. 20, No. 4, pp. 227-236.
Refs: 44
ISSN: 0722-1541 CODEN: NERVDI

COUNTRY: Germany

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery

LANGUAGE: German

SUMMARY LANGUAGE: English; German

ENTRY DATE: Entered STN: 28 Jun 2001
Last Updated on STN: 28 Jun 2001

AB Most of the commonly used antiparkinsonian drugs show neuroprotective potency when tested in tissue culture or animal models. Neuroprotection consists of measures which lead to prevention or delay of neuronal cell death. So far, there are no clinical studies which show undoubtedly neuroprotection. Nonetheless, there are 3 PET- or SPECT-controlled studies with ropinirole, pergolide and promipexole finished which were designed to prove neuroprotection while taking dopamine agonists. This paper will further introduce studies with selegiline and NMDA receptor antagonists which indicate possible neuroprotection. Experimental data suggest studies with radical scavengers, coenzyme Q, iron chelators or antiapoptotic drugs such as flupirtine. Taking all consisting data into account we recommend to treat early Parkinsonism with a combination of selegiline, NMDA receptor antagonists and dopamine agonists.

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STN DUPLICATE 40

ACCESSION NUMBER: 2001:330967 BIOSIS

DOCUMENT NUMBER: PREV200100330967

TITLE: Quick titration of pergolide in cotreatment with domperidone is safe and effective.

AUTHOR(S): Jansen, Paul A. F. [Reprint author]; Herings, Ron M. C.; Samson, Monique M.; De Vreede, Paul L.; Schuurmans-Daemen, Lily M. P. J.; Hovestadt, Ad; Verhaar, Harald J. J.; Van Laar, Teus

CORPORATE SOURCE: Department of Geriatrics, University Medical Center Utrecht, W 01.209, 3508 GA, Utrecht, Netherlands

SOURCE: Clinical Neuropharmacology, (May-June, 2001) Vol. 24, No. 3, pp. 177-180. print.
CODEN: CLNEDB. ISSN: 0362-5664.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 11 Jul 2001

Last Updated on STN: 19 Feb 2002

AB The purpose of the study was to analyze efficacy and safety of quick pergolide titration combined with domperidone. In an open-label prospective study, pergolide was titrated in 16 days to a maximum of 3 mg/d doses as adjunctive treatment to L-Dopa in 10 elderly patients with Parkinson's disease. Sixty milligrams domperidone was started 2 days before and continued during the pergolide titration period to prevent side effects. Adverse events were studied for 6 weeks. Efficacy was measured with the motor part ("on" condition) of the Unified Parkinson's Disease Rating Scale (UPDRS), the 2-minute walking test, the Timed Up and Go test, and the Postural-Locomotor-Manual test. After quick titration of pergolide with domperidone cotreatment, no symptomatic side effects were seen except for lightheadedness in one patient, which disappeared after dose reduction. The UPDRS motor score improved significantly from 21+-8 at baseline to 16+-7 and 12+-7 after 1 and 2 weeks, respectively. The 2-minute walking distance improved significantly from 123+-36 m at baseline to 136+-41 m after 6 weeks. The Timed Up and Go and Postural-Locomotor-Manual test results, overall, did not show significant changes. Quick titration of pergolide to a maximum of 3 mg/d with domperidone cotreatment is safe and effective. Therefore, we recommend domperidone cotreatment in the titration period to prevent unnecessary failure of dopamine agonist treatment because of adverse effects.

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ACCESSION NUMBER: 2002437019 EMBASE
TITLE: Pergolide mesilate may improve fatigue in patients with Parkinson's disease.
AUTHOR: Abe, Kazuo, Dr. (correspondence); Takanashi, Mayako; Yanagihara, Takehiko; Sakoda, Sabro
CORPORATE SOURCE: Department of Neurology, Osaka Univ. Grad. School of Medicine, 2-2 Yamadaoka, Suita, Osaka 565-0871, Japan. abe@neuro.med.osaka-u.ac.jp
SOURCE: Behavioural Neurology, (2001) Vol. 13, No. 3-4, pp. 117-121.
Refs: 19
ISSN: 0953-4180 CODEN: BNEUEI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Dec 2002
Last Updated on STN: 19 Dec 2002

AB Objectives: Fatigue is a complaint frequently encountered among patients with Parkinson's disease (PD). Considering the possible relationship between fatigue and dopaminergic dysfunction, we investigated the effect of pergolide mesilate (a D2 and D1 dopamine receptor agonist) and bromocriptine (a D2 selective dopamine receptor) in patients with PD. Methods: We evaluated 41 patients with PD and controls. We assessed the degree of fatigue by using a fatigue scale. The severity of PD was evaluated by the Hoehn and Yahr Scale and the unified Parkinson's disease rating scale (UPDRS). Results: After five weeks from prescription, patients taking pergolide mesilate showed significant improvement in the fatigue scale (from 5.1 ± 0.7 to 4.4 ± 0.55 , $p < 0.05$,) but patients taking bromocriptine did not (from 4.8 ± 0.9 to 4.7 ± 0.8). Conclusions: Our study suggested the possibility of functional correlation between fatigue and D1 receptor in patients with PD.

L9 ANSWER 58 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 42

ACCESSION NUMBER: 2001:159453 BIOSIS
DOCUMENT NUMBER: PREV200100159453
TITLE: Switching from pergolide to pramipexole in patients with Parkinson's disease.
AUTHOR(S): Hanna, P. A.; Ratkos, L.; Ondo, W. G.; Jankovic, J.
[Reprint author]
CORPORATE SOURCE: Department of Neurology, Parkinson's Disease Center and Movement Disorders Clinic, Baylor College of Medicine, 6550 Fannin St., No. 1801, Houston, TX, 77030, USA
SOURCE: Journal of Neural Transmission, (January 24, 2001) Vol. 108, No. 1, pp. 63-70. print.
CODEN: JNGSE8. ISSN: 0300-9564.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Mar 2001
Last Updated on STN: 15 Feb 2002

AB Objective/Background. To compare the safety and efficacy of pramipexole and pergolide in the treatment of mild to moderate Parkinson's disease (PD). In contrast to pergolide, a D1 and D2 dopamine agonist, pramipexole is a nonergoline dopamine agonist with D2 and preferential D3 dopamine receptor activity. This selective activity may result in clinically different effects. No prospective head-to-head comparison studies of pergolide and pramipexole

have been reported. Methods. Patients with PD who were maintained on an optimal dose of pergolide were converted to pramipexole, typically over a one-month period. Clinical assessments were performed just prior to conversion and after an optimal dose of pramipexole was achieved. Results. Twenty-five patients were converted from pergolide to pramipexole during the period of July, 1997 to January, 1999. Three patients were lost to follow-up, and one patient died. Of the remaining 21 patients there were 11 men and 10 women, mean age was 67.3 years \pm 10.0 (range 51-84). Mean duration of symptoms prior to conversion was 12.5 years \pm 3.4 (range 5-19). All patients (except one) were on concomitant carbidopa/levodopa and experienced motor fluctuations. After a mean follow-up of 5.9 \pm 2.9 months on pramipexole, the mean levodopa daily dose was reduced from 618.7 mg to 581.2 mg (16.5% reduction, p = 0.61). The mean daily doses of pergolide and pramipexole (in milligrams per day) were 2.1 \pm 1.5 (0.15-6) and 3.2 \pm 1.1 (0.75-6) respectively. Thirteen patients (62%) reported overall improvement (subjective global response) on pramipexole as compared to pergolide, 5 (24%) were unchanged and 3 (14%) reported worsening. Eighteen of the 21 patients (86%) remained on pramipexole after the study period. Although there was a slight trend toward improved scores on pramipexole, the difference was not statistically significant. Conclusion. This open label study failed to provide evidence of superior efficacy of either dopamine agonist. It is possible, however, that while some patients may benefit more from either pergolide or pramipexole, other patients may obtain additional benefit from other DA agonists or combination therapy. Future randomized, controlled, double-blinded therapeutic trials are needed to determine which, if any, dopamine agonist is superior in the treatment of PD.

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ACCESSION NUMBER: 2001183665 EMBASE

TITLE: [Clinical evidence with piribedil in Parkinson's disease].
Preuves cliniques de l'efficacite du piribedil dans la maladie de Parkinson.

AUTHOR: Ziegler, M. (correspondence)

CORPORATE SOURCE: Unite James Parkinson, Hopital Leopold Bellan, 19-21 rue Vercingetorix, 75014 Paris, France.

SOURCE: Disease Management and Health Outcomes, (2001)
Vol. 9, No. SPEC. ISS. 1, pp. 49-58.
Refs: 17
ISSN: 1173-8790 CODEN: DMHOFV

COUNTRY: New Zealand

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery

LANGUAGE: French

SUMMARY LANGUAGE: English; French

ENTRY DATE: Entered STN: 7 Jun 2001
Last Updated on STN: 7 Jun 2001

AB Piribedil, a dopamine agonist and non-ergot compound, is indicated in the treatment of Parkinson's disease. Several studies have demonstrated the efficacy of this agent in tremor and parkinsonian symptoms when administered orally as well as by intravenous injection. The average daily dosage of piribedil in the treatment of Parkinson's disease is 207mg. In an open-label, multicentre study of 113 patients treated for 3 months, a 41% improvement on the Webster scale clearly demonstrated the antiparkinsonian effects of piribedil monotherapy. Another more recent, double-blind study versus placebo in 115 patients without fluctuations in symptoms treated with 400

mg/day of levodopa evaluated the effect of the piribedil/levodopa association over a period of 6 months. At the end of the treatment period, the number of responders, defined as patients showing a 30% improvement in the Unified Parkinson's Disease Rating Scale (UPDRS) motor score, was statistically greater in the piribedil group (56%) than in the placebo group (37%) ($p = 0.017$). As a monotherapy in the initial treatment of Parkinson's disease, piribedil has been shown to be effective against tremor, akinesia and rigidity, and could postpone the need to introduce levodopa. As with all dopamine agonists, when piribedil is administered early in association with levodopa, lower dosages of both drugs can be used. This strategy delays the development of motor complications. The recommended dosage is 50mg of piribedil for 200mg of levodopa. In advanced stages of the disease, piribedil can be used to improve fluctuations and dyskinesia, although no studies have as yet been carried out to demonstrate its efficacy in these conditions. A precise dopamine agonist dosage equivalency scale has been determined to allow these agents to be used as substitutes: bromocriptine 10mg = ropinirole 6mg = pergolide 1mg. Although no data has as yet been published regarding the equivalent dose of piribedil, we propose that piribedil 50mg is equivalent to bromocriptine 10mg. As with bromocriptine and ropinirole, piribedil can be used as an initial treatment as well as in association with levodopa. Piribedil differs from other dopamine agonists by its affinity for D(2) and D(3) receptors and its non-ergot derivative structure. It is of particular importance that neurologists have a wide range of agonists at their disposal to enable treatment to be adapted to the different stages of Parkinson's disease.

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ACCESSION NUMBER: 2001159743 EMBASE

TITLE: Dopamine agonists.

AUTHOR: Tuite, P., Dr. (correspondence); Ebbitt, B.

CORPORATE SOURCE: UMHC Box 295, University of Minnesota, 420 Delaware Street SE, Minneapolis, MN 55455, United States.

SOURCE: Seminars in Neurology, (2001) Vol. 21, No. 1, pp. 9-14.
Refs: 51
ISSN: 0271-8235 CODEN: SEMNEP

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 17 May 2001
Last Updated on STN: 17 May 2001

AB Dopamine agonists provide an effective means of treating early, middle, and late stages of Parkinson's disease. This article outlines the advantages and disadvantages of dopamine agonists as compared with levodopa therapy. The features and costs of the four Food and Drug Administration-approved agonists (bromocriptine, pergolide, pramipexole, and ropinirole) and apomorphine, another agonist presently under investigation, are discussed.

L9 ANSWER 61 OF 331 MEDLINE on STN DUPLICATE 44

ACCESSION NUMBER: 2000512161 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11068454

TITLE: Wearing-off phenomenon--neurological approach.

AUTHOR: Ishikawa A

CORPORATE SOURCE: Department of Neurology, Nishi-Ojiya National Hospital.

SOURCE: Nippon rinsho. Japanese journal of clinical medicine,
(2000 Oct) Vol. 58, No. 10, pp. 2100-3. Ref: 9
Journal code: 0420546. ISSN: 0047-1852.

PUB. COUNTRY: Japan

DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LANGUAGE: Japanese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200102

ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 1 Feb 2001

AB The mechanism of the wearing-off phenomenon and the method of how to control it by means of anti-parkinsonian medications is described. To control the wearing-off phenomenon, it is useful to administer L-dopa before eating because absorption of L-dopa is less when competing with amino acids. Administration of L-dopa four or five times a day is also useful. Dopamin agonists(e.g., bromocriptine, pergolide, talipexole, and cabergoline), and monoamine oxidase inhibitors(e.g., selegiline) control the wearing-off phenomenon, and may also suppress its occurrence. As a specific method for controlling the wearing-off phenomenon, continuous administration of anti-parkinsonian drugs by the intra-alimentary tract or a subcutaneous injection is useful. It is important to avoid early wearing-off phenomenon when treating patients with Parkinson's disease.

L9 ANSWER 62 OF 331 MEDLINE on STN

ACCESSION NUMBER: 2000512155 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11068448

TITLE: The new Parkinson's disease drugs.

AUTHOR: Hasegawa K

CORPORATE SOURCE: Division of Neurology, Sagamihara National Hospital.

SOURCE: Nippon rinsho. Japanese journal of clinical medicine,
(2000 Oct) Vol. 58, No. 10, pp. 2066-71. Ref: 13
Journal code: 0420546. ISSN: 0047-1852.

PUB. COUNTRY: Japan

DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LANGUAGE: Japanese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200102

ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 1 Feb 2001

AB The purpose of the new drugs for Parkinson's disease is control of the long-term levodopa treatment syndromes, especially wearing-off phenomenon and dyskinesia. Therefore, they show long T1/2. Most of them are classified into dopamine agonists. Others are monoamine oxidase B inhibitor and cathecole-o-methyltransferase inhibitor. Marketed dopamine agonists are bromocriptine, pergolide, talipexole, and cabergoline in Japan. Except talipexole, they are all ergot alkaloid derivatives. Their affinity for dopamine receptor is D2 group, and their T1/2 are longer than levodopa. Bromocriptine is an oldest dopamine agonist. Other 3 drugs and bromocriptine had made each other double blinded cross over trial previously. The result of double blinded studies show that their efficacy for PD treatment were equal, 40-50% patients with PD. However, in clinical usage, some difference is observed as described below. Efficacy of pergolide is strong compared with bromocriptine; however, pergolide is easy to arise dyskinesia. Talipexole is strong in the hypnosis effect. As for cabergoline, it takes

long time to show medical effect, so that it is expected to control wearing-off phenomenon. Monoamine oxidase B inhibitor, Selegiline, is useful as an economizer effect to levodopa. As for the catechole-o-methyltransferase inhibitor (COMT-I) will be make double-blinded trial in future. The efficacy for PD treatment of COMT-I is prolonged levodopa effect for PD, so that wearing-off phenomenon will be controlled. To use these drugs successfully is important with the treatment of PD. In the future, the development of the cause therapy in addition to the systematic therapy is wanted.

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STN DUPLICATE 45

ACCESSION NUMBER: 2000:511088 BIOSIS
DOCUMENT NUMBER: PREV200000511088
TITLE: Acute orthostatic hypotension when starting dopamine agonists in Parkinson's disease.
AUTHOR(S): Kujawa, Kathy [Reprint author]; Leurgans, Sue; Raman, Rema; Blasucci, Lucy; Goetz, Christopher G.
CORPORATE SOURCE: Department of Neurology, Glenbrook Hospital, 2100 Pfingsten Rd, Glenview, IL, 60025, USA
SOURCE: Archives of Neurology, (October, 2000) Vol. 57, No. 10, pp. 1461-1463. print.
CODEN: ARNEAS. ISSN: 0003-9942.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Nov 2000
Last Updated on STN: 12 Feb 2002

AB Objective: To study the frequency and severity of acute orthostatic hypotension (OH) in patients with Parkinson's disease who are starting dopamine agonist therapy. Patients and Methods: In the context of an outpatient clinical practice, 29 consecutive patients with Parkinson's disease who were starting dopamine agonist therapy were brought into the clinic for their first dose of agonist. After a baseline supine and standing blood pressure assessment, patients were given a test dose of either pergolide mesylate (0.025, 0.05, 0.125, or 0.25 mg), pramipexole dihydrochloride (0.125 mg), or ropinirole hydrochloride (0.125 or 0.25 mg). At 3 selected times, blood pressure readings were repeated in the supine and standing positions. Main Outcome Measure: Orthostatic hypotension was defined as a drop in either systolic blood pressure of more than 25 mm Hg or diastolic pressure of more than 10 mm Hg. Patients with OH before the administration of the dopamine agonist were excluded. Results: Ten subjects (34%) met the criteria for acute OH. There was no evidence that OH was related to the use of a specific dopamine agonist or the concurrent use of levodopa. Of the patients who met the criteria for OH, only 3 (30%) had symptoms of OH, such as lightheadedness or general malaise. Conclusions: Acute OH occurs frequently when starting dopamine agonist therapy in Parkinson's disease, but is frequently not appreciated by patients. Knowledge of acute blood pressure responses may be useful when making decisions regarding agonist titration schedules in clinical practice.

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STN DUPLICATE 46

ACCESSION NUMBER: 2001:240218 BIOSIS
DOCUMENT NUMBER: PREV200100240218
TITLE: Sleep attacks and Parkinson's disease treatment.
AUTHOR(S): Ferreira, J. J.; Galitzky, M.; Montastruc, J. L.; Rascol, O. [Reprint author]
CORPORATE SOURCE: Service de Pharmacologie Medicale et Clinique, Faculte de Medecine, 31073, Toulouse Cedex, France
rascoll@cict.fr
SOURCE: Lancet (North American Edition), (15 April, 2000)

Vol. 355, No. 9212, pp. 1333-1334. print.
ISSN: 0099-5355.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 16 May 2001
Last Updated on STN: 18 Feb 2002

AB Three patients with Parkinson's disease had so-called sleep attacks at the wheel while taking bromocryptine, lisuride pergolide, or piribedil. We believe that all dopamine agonists can induce sleep attacks.

L9 ANSWER 65 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 47
ACCESSION NUMBER: 2000:284939 CAPLUS
DOCUMENT NUMBER: 133:217177
TITLE: Sleep attacks (sleep episodes) with pergolide
AUTHOR(S): Schapira, A. H. V.
CORPORATE SOURCE: University Department of Clinical Neurosciences, Royal Free and University College Medical School and Institute of Neurology, London, UK
SOURCE: Lancet (2000), 355(9212), 1332-1333
CODEN: LANCAO; ISSN: 0140-6736
PUBLISHER: Lancet Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A discussion, with 3 refs., of the increased sedation, somnolence, and sleep episodes that seem to occur in patients with Parkinson's disease treated with some, if not all, dopamine agonists (including pergolide) and dopaminergic treatment. Patients at risk of sleep episodes can be identified by well-chosen questions, and the syndrome could be managed by appropriate measures, including dose reduction

OS.CITING REF COUNT: 22 THERE ARE 22 CAPLUS RECORDS THAT CITE THIS RECORD (22 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 66 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:3254 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 37-14220
TITLE: Sleep attacks (sleep episodes) with pergolide
AUTHOR(S): Schapira, A. H.
CORPORATE SOURCE: Univ. Dept. of Clin. Neurosci., Royal Free and Univ. Coll. of Med. Sch., and Inst. of Neurol., London NW3 2PF, England Internet: schapira@rfhsm.ac.uk
SOURCE: Lancet (England), (Apr 15 2000) Vol. 355, pp. 1332-1333. 3 Refs.
CODEN: LANCAO. ISSN: 0023-7507.

DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 2000:14219
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB Two cases of a 57 yr old woman and a 61 yr old man who experienced increased somnolence and episodes of unplanned sleep after receiving 4.5-5 mg of oral pergolide daily for a few wk to 1 month as therapy for Parkinson's disease are reported. The male patient would fall asleep while speaking, watching television, eating and drinking, and depending on circumstances, sleep lasted up to several min or h. There were no neurological sequelae. The female patient's sleep episodes would occur at any time of day and in various circumstances. In both patients, pergolide was lowered to 3 mg daily with cessation of sleep

episodes.
Elizabeth G. Rudnic

L9 ANSWER 67 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 48

ACCESSION NUMBER: 2000:373565 BIOSIS
DOCUMENT NUMBER: PREV200000373565
TITLE: Effects of chronic levodopa and pergolide treatment on
cortical excitability in patients with Parkinson's disease:
A transcranial magnetic stimulation study.
AUTHOR(S): Strafella, A. P. [Reprint author]; Valzania, F.; Nasseti,
S. A.; Tropeani, A.; Bisulli, A.; Santangelo, M.;
Tassinari, C. A.
CORPORATE SOURCE: Montreal Neurological Institute, McGill University, Webster
2B, 3801, Rue University, Montreal, PQ, H3A 2B4, Canada
SOURCE: Clinical Neurophysiology, (July, 2000) Vol. 111,
No. 7, pp. 1198-1202. print.
ISSN: 1388-2457.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Aug 2000
Last Updated on STN: 8 Jan 2002

AB Objectives: Transcranial magnetic stimulation was used to assess the
effects of chronic levodopa and pergolide treatment on motor
cortex excitability in Parkinson disease (PD). Methods: Motor
thresholds, intracortical inhibition and facilitation were studied at
baseline and after 6 and 12 months of therapy in 10 PD patients and
compared to 7 age-matched controls. Results: At baseline, there was
significantly less intracortical inhibition with only a slight reduction
of intracortical facilitation in PD as compared to controls. Relative to
pretreatment condition, levodopa restored intracortical inhibition for 12
months while pergolide did not. Intracortical facilitation was
always within the normal range. Motor thresholds were unchanged in both
groups of patients over 12 months. Clinically, levodopa and
pergolide improved motor Unified Parkinson's disease
rating scale (UPDRS) scores at 6 months but only levodopa maintained
benefit at 12 months as compared to baseline. Conclusions: Levodopa and
pergolide differentially affected cortical inhibitory circuits at
12 months. The progressive deterioration of restored intracortical
inhibition with pergolide may be due to the development of
tolerance and down-regulation of dopamine receptors.

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STN DUPLICATE 49

ACCESSION NUMBER: 2001:33644 BIOSIS
DOCUMENT NUMBER: PREV200100033644
TITLE: Comparative effects of repeated administration of dopamine
agonists on circling behavior in rats.
AUTHOR(S): Prikhojan, A.; Brannan, T.; Yahr, M. D. [Reprint author]
CORPORATE SOURCE: Department of Neurology, Mount Sinai School of Medicine,
One Gustave Levy Place, New York, NY, 10029, USA
melvin.yahr@smtplink.mssm.edu
SOURCE: Journal of Neural Transmission, (October 25, 2000
) Vol. 107, No. 10, pp. 1159-1164. print.
CODEN: JNGSE8. ISSN: 0300-9564.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Jan 2001
Last Updated on STN: 12 Feb 2002

AB A paucity of studies are available concerning the comparative therapeutic
effectiveness of presently available dopamine agonist agents in the
control of Parkinson symptoms. To provide a basis for resolving

this issue, we measured the circling response in unilaterally nigrotomized (6-OHDA) rats following the administration of ropinirole, pramipexole, pergolide, bromocriptine, and cabergoline. Cabergoline, and to a lesser extent pergolide, produced the most vigorous and longest lasting circling response. This response was sustained with administration of these agents over a nine day period. Bromocriptine, pramipexole and ropinirole were all less effective. These results suggest that dopamine agonists whose effect is primarily on D1 and D2 receptors are more effective than those whose actions do not include D1 activation.

L9 ANSWER 69 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:328893 CAPLUS
TITLE: X-ray structural studies of ergoline derivatives with dopamine agonist activity.
AUTHOR(S): Klein Stevens, Cheryl L.; Zhu, Naijue; Johnson, L'Aurelle
CORPORATE SOURCE: Department of Chemistry, Xavier University of Louisiana, New Orleans, LA, 70125, USA
SOURCE: Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, March 26-30, 2000 (2000), CHED-751. American Chemical Society: Washington, D. C.
CODEN: 69CLAC
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB Dopamine agonists are compds. that bind to the dopamine receptor and cause a response similar to that of dopamine itself. These compds. show promise in the treatment of Parkinson's disease which is caused by a shortage of dopamine in the brain. The ergolines are a conformationally restrained class of dopamine agonists with the dopamine connectivity frozen within the mols. We report here the x-ray crystal structure of four ergoline derivs. These are terguride hydrogen maleate, mesulergine hydrochloride, pergolide methanesulfonate, and dihydroergocriptine. Each of these compds. contains the ergot skeleton with various substituents that cause the compds. to have varying degrees of pharmacol. activity. We will compare the activities as well as the structural characteristics of these compds. in an effort to correlate the structures with the dopaminergic activities.

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DUPLICATE 50

ACCESSION NUMBER: 2000260720 EMBASE
TITLE: The use of dopamine agonists in very elderly patients with Parkinson's disease.
AUTHOR: Shulman, Lisa M.; Minagar, Alireza; Rabinstein, Alejandro; Weiner, William J., Dr. (correspondence)
CORPORATE SOURCE: Department of Neurology, Univ. of Miami School of Medicine, Miami, FL, United States.
AUTHOR: Weiner, William J., Dr. (correspondence)
CORPORATE SOURCE: Department of Neurology, Univ. of Miami School of Medicine, 1501 N.W. 9 Avenue, Miami, FL 33136, United States.
AUTHOR: Weiner, William J., Dr. (correspondence)
CORPORATE SOURCE: Department of Neurology, University of Miami School of Med., 1051 N.W. 9 Avenue, Miami, FL 33136, United States.
SOURCE: Movement Disorders, (2000) Vol. 15, No. 4, pp. 664-668.
Refs: 34
ISSN: 0885-3185 CODEN: MOVDEA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 020 Gerontology and Geriatrics
037 Drug Literature Index

038 Adverse Reactions Titles
008 Neurology and Neurosurgery

LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 10 Aug 2000
Last Updated on STN: 10 Aug 2000

AB Background: Controversy exists regarding the use of dopamine receptor agonists in elderly patients with Parkinson's disease because of concern about a high rate of intolerable side effects. Methods: A retrospective chart review was used to examine our experience with dopamine agonist use in the very elderly by identifying patients in our Parkinson's disease database who were over the age of 80 years and who had received agonists. Sixty-nine patients were identified who had 120 separate trials of agonist therapy. Successful treatment with the agonist was defined as maintenance of the agonist for a minimum of 6 months. Results: The overall success rate among the very elderly for an agonist trial was 46%. Success rates for individual agonists were 15 of 27 (56%) bromocriptine, 18 of 34 (53%) pergolide, 17 of 43 (40%) pramipexole, and 5 of 16 (31%) ropinirole. In successful trials with bromocriptine, the mean daily dose was 12.8 mg, mean duration of treatment was 40 months, and mean age at drug initiation was 82 years; for pergolide it was 1.8 mg, 32 months, and 83 years; for pramipexole 2.7 mg, 14 months, and 83 years, and for ropinirole 10.6 mg, 11 months, and 83 years. Conclusion: This study demonstrated that therapeutic dosages of dopamine agonists were well tolerated by 46% of very elderly patients who received a trial of an agonist. These results indicate that dopamine receptor agonist therapeutic trials are warranted in selected very elderly patients.

L9 ANSWER 71 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 51

ACCESSION NUMBER: 2000:639883 CAPLUS
DOCUMENT NUMBER: 134:125417
TITLE: Treatment of motor complications in advancing Parkinson's disease: Which drugs and when?
AUTHOR(S): Ahlskog, J. Eric
CORPORATE SOURCE: Department of Neurology, Mayo Clinic, Rochester, MN, 55905, USA
SOURCE: Formulary (2000), 35(8), 654-656, 661-664, 667-668
CODEN: FORMF9; ISSN: 1082-801X
PUBLISHER: Advanstar Communications, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 93 refs. After several years of Parkinson's disease (PD), most levodopa-treated patients begin to experience motor complications, ie, clin. fluctuations and dyskinesias. The motor fluctuations relate to the development of short-duration levodopa responses, or "wearing-off" of the levodopa effect. This should probably be treated initially with levodopa adjustment. Subsequently, a dopamine agonist (typically pergolide, pramipexole, or ropinirole) or the COMT inhibitor entacapone may be added. The advantage of entacapone is an immediate response, whereas the disadvantage is a greater likelihood of exacerbating dyskinesias. Another COMT inhibitor, tolcapone, is also efficacious but is a second-line drug because of its potential for serious, albeit rare, hepatopathy. With each form of adjunctive therapy, further adjustment of levodopa dosage is often necessary. Both classes of adjunctive therapy may be concomitantly employed. However, with increasing polypharmacy, psychosis or orthostatic hypotension is an occasional problem. Dyskinesias are best treated with levodopa dose reduction, as tolerated. Amantadine may be added in select refractory cases.

REFERENCE COUNT: 93 THERE ARE 93 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ACCESSION NUMBER: 2000260715 EMBASE
TITLE: Chronic effects of dopaminergic replacement on cognitive function in Parkinson's disease: A two-year follow-up study of previously untreated patients.
AUTHOR: Kulisevsky, Jaime, Dr. (correspondence)
CORPORATE SOURCE: Movement Disorders Unit, Department of Neurology, Sant Pau Hospital, Sant Antoni M. Claret 167, 08025 Barcelona, Spain
AUTHOR: Garcia-Sanchez, Carmen; Berthier, Marcelo L.; Barbanoj, Manel; Pascual-Sedano, Berta; Gironell, Alexandre; Estevez-Gonzalez, Armando
SOURCE: Movement Disorders, (2000) Vol. 15, No. 4, pp. 613-626.
Refs: 92
ISSN: 0885-3185 CODEN: MOVDEA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 10 Aug 2000
Last Updated on STN: 10 Aug 2000

AB Background: The cognitive effects of dopaminergic treatment in Parkinson's disease (PD) are still controversial. Objective: To evaluate, in previously untreated patients with PD, whether chronic dopaminergic stimulation produces significant cognitive changes; whether they are sustained beyond the period of a few months; and whether the cognitive status of two motor-comparable groups is differently affected by levodopa and pergolide. Design and Subjects: Parallel, randomized open study with blind neuropsychologic evaluation of 20 consecutive de novo patients with PD before and 3, 6, 12, 18, and 24 months after monotherapy with levodopa (n = 10) or pergolide (n = 10; 6-month monotherapy; pergolide + levodopa thereafter). Results: Both treatments were associated with a significant improvement in motor scores and in tests assessing learning and long-term verbal and visual memory, visuospatial abilities, and various frontal tasks. While improvement in motor scores persisted, improvement in activities of daily living and in semantic fluency. Luria's rhythm and motor and long-term memory tests was not sustained at the 24-month examination. Further, performance on attentional, short-term memory, and the Stroop tests did not change over the course of the study. Conclusions: Both treatments were associated with incomplete but long-lasting (18 mos) improvement in many cognitive tasks which declined thereafter, suggesting that dopaminergic replacement is not enough to compensate for all cognitive deficits of PD.

L9 ANSWER 73 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 53

ACCESSION NUMBER: 2000397183 EMBASE
TITLE: Pergolide-induced dyspnea, bilateral pleural effusion and peripheral edema.
AUTHOR: Varsano, S., Dr. (correspondence); Gershman, M.; Hamaoui, E.
CORPORATE SOURCE: Department of Pulmonary Medicine, Sapir Medical Center, Meir General Hospital, 44281 Kfar-Sava, Israel. varsanos@bezeqint.net

SOURCE: Respiration, (2000) Vol. 67, No. 5, pp. 580-582.
Refs: 9
ISSN: 0025-7931 CODEN: RESPBD
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 14 Dec 2000
Last Updated on STN: 14 Dec 2000

AB A patient with severe Parkinson's disease presented with increasing dyspnea, bilateral pleural effusion and peripheral edema that were refractory to diuretic therapy and were first misdiagnosed as signs of right-sided heart failure. Pergolide was the only culprit for this devastating condition and on its discontinuation all signs of fluid retention resolved. In this report, drug reactions to ergots and dopamine agonists are discussed. Copyright (C) 2000 S. Karger AG, Basel.

L9 ANSWER 74 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 54

ACCESSION NUMBER: 2000395778 EMBASE
TITLE: [Akathisia secondary to tolcapone. Report of a case].
Acatisia secundaria a tolcapone. Reporte de un caso.
AUTHOR: Colorado-Ochoa, H. (correspondence)
CORPORATE SOURCE: Hospital ISSSTE, F. Magon 657-1 esq. de a llave, C.P. 91910 Veracruz Ver, Mexico.
SOURCE: Gaceta Medica de Mexico, (2000) Vol. 136, No. 5, pp. 505-509.
Refs: 21
ISSN: 0016-3813 CODEN: GMMEAK
COUNTRY: Mexico
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: Spanish; Castilian
SUMMARY LANGUAGE: English; Spanish; Castilian
ENTRY DATE: Entered STN: 13 Dec 2000
Last Updated on STN: 13 Dec 2000

AB The purpose of this work is to report a case of tolcapone-induced akathisia. A 39-year-old woman with Parkinson's disease, Hohen-Yahr IV, Webster 18 points with 10 years within onset presented lack of clinical response to levodopa-carbidopa, pergolide, selegiline and trihexiphenidyl, showing freezing and wearing-off phenomena and choreic dyskinetic abnormal movements of the upper and lower extremities, during the six months previous to her evaluation. Her hepatic function was normal. Levodopa-carbidopa and selegiline were diminished to add tolcapone, as described elsewhere. During the first three weeks, the patient showed marked clinical improvement of previous complications and sustained improvement during 12.5 weeks. At the 13th week of tolcapone therapy the patient developed constant orofacial, trunk, and superior and lower limb involuntary movements associated to lack of stand still. Laboratory tests showed discrete elevation of oxaloacetic-glutamic transaminase, direct bilirubin, indirect bilirubin, and alkaline phosphatase. Electroencephalogram and CT scan were normal. Tolcapone therapy was finished, and levodopacarbidopa, pergolide and selegiline were diminished, procuring the disappearance of akathisia within 72 h.

L9 ANSWER 75 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 55

ACCESSION NUMBER: 2001016074 EMBASE
TITLE: [Dopaminergic agonists in idiopathic Parkinson's disease treatment].
Les agonistes dopaminergiques dans le traitement de la maladie de Parkinson.
AUTHOR: Supiot, F.; Sternon, J. (correspondence); Zegers de Beyl, D.
CORPORATE SOURCE: Route de Lennik 808 bte 612, 1070 Bruxelles, France.
SOURCE: Revue Medicale de Bruxelles, (2000) Vol. 21, No. 6, pp. 493-499.
Refs: 19
ISSN: 0035-3639 CODEN: RMBXA7
COUNTRY: Belgium
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: French
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 1 Feb 2001
Last Updated on STN: 1 Feb 2001

AB After levodopa, dopaminergic agonists are the most powerful agents in idiopathic Parkinson's disease treatment. Used in monotherapy or rather in early combination with levodopa, they allow a dramatic reduction of long-term motor side effects of the latter: Onset and peak-dose dyskinesias, early morning dystonias. Their gastro-intestinal (nauseas) and moreover psychiatric (confusion and hallucinations) side effects limit their use, notably in geriatric populations. Superiority of so-called "second generation" agonists (ropinirole, pramipexole) on "first generation" agonists (bromocriptine, pergolide) remains to be proved.

L9 ANSWER 76 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 56

ACCESSION NUMBER: 2001:50015 CAPLUS
DOCUMENT NUMBER: 135:116244
TITLE: Pharmacokinetic optimization of dopamine receptor agonist therapy for Parkinson's disease
AUTHOR(S): Contin, Manuela; Riva, Roberto; Albani, Fiorenzo; Baruzzi, Agostino
CORPORATE SOURCE: Laboratory of Clinical Neuropharmacology, Institute of Neurology, University of Bologna, Bologna, Italy
SOURCE: CNS Drugs (2000), 14(6), 439-455
CODEN: CNDREF; ISSN: 1172-7047
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 147 refs. Dopamine receptor agonists were originally developed as adjunctive therapies to "smooth out" motor response fluctuations to levodopa in patients with advanced Parkinson's disease. However, they are now used in the early stages of the disease, in monotherapy or combination with low doses of levodopa, to delay the onset of levodopa therapy and its complications. Oral dopamine agonists currently available worldwide for Parkinson's disease include the older ergot derivs. bromocriptine and pergolide and the second generation non-ergoline compds. ropinirole and pramipexole. Other dopamine agonists that are used less frequently include cabergoline (a new ergoline drug, only recently released in some European countries as an antiparkinsonian drug), lisuride (an ergot derivative) and piribedil (an older non-ergot compound). Data on the pharmacokinetics of oral dopamine agonists, especially the older ergot derivs., are scarce and mostly

refer to small groups of healthy young individuals. All these agents, with the exception of pramipexole, are subject to extensive enterohepatic first-pass metabolism. Their bioavailability is low and shows high intra- and interindividual variability. The pharmacodynamic properties of dopamine agonists relevant to their anti-parkinsonian effect have not been clearly defined. As a result, an optimal dosage schedule for the treatment of Parkinson's disease is generally identified using highly individualized empirical assessment. This involves considerable time expenditure and creates difficulty for patients, who have to follow complex titration schedules. Dopamine agonists appear to have a low potential for pharmacokinetic interaction with levodopa. Few data have been reported on the effect of coadministration on the pharmacodynamics of levodopa. The available data indicate that pergolide and bromocriptine significantly increase the duration of the motor response to levodopa, while baseline motor effects and the magnitude of motor response are substantially unchanged. Cabergoline also significantly prolongs the motor response to a dose of levodopa in patients experiencing motor fluctuations, but baseline motor scores are also significantly improved, suggesting a long-lasting effect. S.c. apomorphine is currently the only non-oral formulation of a dopamine agonist available; it is used as add-on rescue therapy for patients who have advanced Parkinson's disease and a wide spectrum of complex motor, sensory, autonomic and cognitive "wearing-off" phenomena not controlled by optimal oral dopaminergic therapy. Attempts to deliver apomorphine and other soluble dopamine agonists by more practical non-oral routes, such as intranasally or transdermally, have so far been of limited clin. utility or are currently still under investigation.

OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 147 THERE ARE 147 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 77 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 57

ACCESSION NUMBER: 2000274305 EMBASE
TITLE: Pergolide-induced retroperitoneal fibrosis.
AUTHOR: Mondal, B.K., Dr. (correspondence); Suri, S.
CORPORATE SOURCE: Department of Medicine for Elderly, Rotherham District General Hospital, Moorgate Road, Rotherham, South Yorkshire S60 2UD, United Kingdom.
SOURCE: International Journal of Clinical Practice, (2000) Vol. 54, No. 6, pp. 403.
Refs: 3
ISSN: 1368-5031 CODEN: IJCPF9
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Aug 2000
Last Updated on STN: 24 Aug 2000

AB Retroperitoneal fibrosis is a rare complication of pergolide therapy. This complication can be easily missed, so it is essential to have a high index of suspicion. We describe a case of well controlled Parkinson's disease who presented with shortness of breath and oedema.

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STN DUPLICATE 58

ACCESSION NUMBER: 2000:320710 BIOSIS
DOCUMENT NUMBER: PREV200000320710
TITLE: Effects of sub-chronic combined treatment with pergolide
and caffeine on contralateral rotational behavior in
unilateral 6-hydroxydopamine-denervated rats.
AUTHOR(S): Prat, Gemma; Robledo, Patricia; Rubio, Antonia; Barbanoj,
Manel; Jane, Francesc; Casas, Miquel [Reprint author]
CORPORATE SOURCE: Laboratori de Neuropsicofarmacologia, Unitat de
Toxicomanies, Departaments de Psiquiatria i de
Farmacologia, Institut de Recerca de L'Hospital de la Santa
Creu i Sant Pau, Universitat Autònoma de Barcelona,
Hospital de la Santa Creu i Sant Pau, Avgda, St. Antoni Ma
Claret, 167, 08025, Barcelona, Spain
SOURCE: Brain Research, (23 June, 2000) Vol. 868, No. 2,
pp. 376-379. print.
CODEN: BRREAP. ISSN: 0006-8993.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jul 2000
Last Updated on STN: 7 Jan 2002

AB We studied the synergistic effects of pergolide and
bromocriptine with caffeine on turning behavior in 6-OHDA denervated rats.
Both pergolide and bromocriptine were synergistic with caffeine,
and prevented tolerance to caffeine-induced turning. When caffeine was
removed, tolerance to bromocriptine effects was observed for 1 day only,
while no tolerance was observed to pergolide. These results
suggest that caffeine could be useful in the treatment of
Parkinson's disease, preferentially as an adjuvant of mixed
dopaminergic agonists like pergolide.

L9 ANSWER 79 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 59

ACCESSION NUMBER: 2000:370924 CAPLUS
DOCUMENT NUMBER: 133:115407
TITLE: Dopamine agonists and analogues have an
antiproliferative effect on CHO-K1 cells
AUTHOR(S): Maggio, Roberto; Armogida, Marianna; Scarselli, Marco;
Salvadori, Federica; Longoni, Biancamaria; Pardini,
Carla; Chiarenza, Andrea; Chiacchio, Serena; Vaglini,
Francesca; Bernardini, Renato; Colzi, Anna; Corsini,
Giovanni U.
CORPORATE SOURCE: Department of Neuroscience, University of Pisa, Pisa,
Italy
SOURCE: Neurotoxicity Research (2000), 1(4), 285-297
CODEN: NURRFI; ISSN: 1029-8428
PUBLISHER: Harwood Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Epidemiol. studies have shown a reduced incidence of cancer in
Parkinson's disease. Since nearly all parkinsonian
patients with clin. impairment are treated with
L- β -3,4-dihydroxyphenylalanine (L-DOPA) and dopamine (DA)ergic
agonists, a possibility exists that these therapeutic agents can influence
the risk of cancer. The authors studied the antiproliferative effect of
these therapeutic agents (and substances structurally correlated) on
Chinese hamster ovary (CHO)-K1 cell growth. Among the compds. tested,
apomorphine proved to be the most potent inhibitor of CHO-K1 cell growth,
with an EC50 of 3.35 \pm 0.12 μ M. The apomorphine analogs, apocodeine
and hydroxyethylnorapomorphine, were less active as inhibitors of CHO-K1
cell growth. The activity of DA, 6-hydroxydopamine (6-OHDA),
phenylethylamine (PEA), L-DOPA and bromocriptine as antiproliferative was

one order of magnitude lower than that of apomorphine while pergolide was ineffective. To test whether or not the oxidative potential of these compds. was important for their antiproliferative effect, several antioxidants were assayed. Among them, glutathione (GSH) and dithiothreitol (DTT) were effective in reversing the antiproliferative effect of apomorphine, DA, 6-OHDA and PEA, conversely they did not work with bromocriptine. GSH and DTT are sulfhydryl-reducing agents; while their effect could explain the efficacy against apomorphine, DA and 6-OHDA, it is difficult to understand why they should have any effect on PEA as this substance does not react with sulfhydryl groups. The oxidative potential as a mechanism of action was also questioned by the results obtained with dihydrorhodamine 123, a probe that changes its fluorescent emission wave when oxidized. None of the compds., with the exception of 6-OHDA, had any effect on the fluorescent emission wave of the probe at the maximal concns. used to inhibit CHO-K1 cell growth. At concns. five times higher, apomorphine and DA generated reactive oxygen species but PEA and bromocriptine did not. These data demonstrate that the antiproliferative effect of these compds. is not due to their oxidative potential, but another mechanism must be postulated.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 80 OF 331 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:776285 SCISEARCH

THE GENUINE ARTICLE: 363NY

TITLE: Dopamine agonists treatment in Parkinson's disease: Experience with pergolide

AUTHOR: Ruzicka E (Reprint); Jech R; Roth J; Michalcikova B; Mecir P; Volfova M

CORPORATE SOURCE: LF UK & VFN, Ctr Extrapramidovych Onemocneni, Neurol Klin 1, Prague, Czech Republic

COUNTRY OF AUTHOR: Czech Republic

SOURCE: CESKA A SLOVENSKA NEUROLOGIE A NEUROCHIRURGIE, (2000) Vol. 63, No. 5, pp. 283-290. ISSN: 1210-7859.

PUBLISHER: CZECH MEDICAL SOCIETY, SOKOLSKA 31, PRAGUE 2 120 26, CZECH REPUBLIC.

DOCUMENT TYPE: Article; Journal

LANGUAGE: Czech

REFERENCE COUNT: 32

ENTRY DATE: Entered STN: 2000

Last Updated on STN: 2000

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Motor fluctuations and levodopa-induced dyskinesias are critical manifestations of advanced Parkinson's disease. Dopamine agonist drugs have been suggested as treatment for these complications. We report our first experience with pergolide (Permax(R)). The treatment was introduced in 75 patients with Parkinson's disease, in Hoehn & Yahr stages 1 to 4, mean age 57, and mean disease duration 9 years. 71 from 75 patients were treated with levodopa for 6 years on average, most of them suffering from motor fluctuations and dyskinesias. In four patients with early disease, pergolide was used as their first dopaminergic treatment. Pergolide was introduced in a progressive dosage up to a fully effective dose (mean, 2.3 mg daily). In retrospective evaluation, motor status and functional abilities improved in 66 of 75 patients (88 %). The mean levodopa dose decreased from 877 to 805 mg daily (by 8 %). Adverse side effects of pergolide were recorded in 36 (48 %) patients, typically transitory dizziness, nausea, or deterioration of dyskinesias. In 7 cases

(8 %) pergolide had to be discontinued, mostly because of nausea, dizziness, or anxiety. The treatment was successful in all four patients to whom pergolide was given in monotherapy. A prospective evaluation was performed in a sub-group of 23 patients. After 3 months, mean UPDRS (Unified Parkinson's Disease Rating Scale) scores decreased significantly: motor score in the "on" state, from 18.7 to 7.7 points ($p < 0.0001$), activities of daily living score, from 8.8 to 4.9 ($p < 0.0001$) and motor complications score, from 4.0 to 2.2 ($p < 0.001$). According to the patients' diaries, the daily duration of deteriorated locomotion decreased by 53 %, from 6.6 to 3.1 hours. In conclusion, our experience demonstrates pergolide as highly efficient treatment in combination with levodopa in advanced Parkinson's disease. Pergolide significantly improves the patients' motor status and their ability for daily living activities, and decreases motor fluctuations. In some patients, adverse side-effects appears which are mostly transient and do not require discontinuation of treatment.

L9 ANSWER 81 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 60

ACCESSION NUMBER: 2001:57104 BIOSIS
DOCUMENT NUMBER: PREV200100057104
TITLE: A comparison of dopamine agonists and catechol-O-methyltransferase inhibitors in Parkinson's disease.
AUTHOR(S): Inzelberg, Rivka [Reprint author]; Carasso, Ralph L.; Schechtman, Edna; Nisipeanu, Puiu
CORPORATE SOURCE: Department of Neurology, Hillel Yaffe Medical Center, Hadera, 38100, Israel
SOURCE: Clinical Neuropharmacology, (September-October, 2000) Vol. 23, No. 5, pp. 262-266. print.
CODEN: CLNEDB. ISSN: 0362-5664.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jan 2001
Last Updated on STN: 12 Feb 2002

AB To compare the efficacy and tolerability of three dopamine agonists- pergolide (PRG), pramipexole (PRX), and ropinirole (ROP)-and two catechol-O-methyltransferase (COMT) inhibitors-tolcapone (TOL) and entacapone (ENT)-as add-on therapies to levodopa (L-Dopa) in Parkinson's disease, we analyzed randomized, double-blind, placebo-controlled, multicenter studies. To our knowledge, they had not yet been evaluated in comparison with each other. Statistical analyses used odds ratios, numbers needed to harm, and Fisher's inverse chi2 method. Seven studies meeting the inclusion criteria included treatment of 1,756 patients. The common efficacy measures were the reduction of L-Dopa dose and "off" duration. The reported reduction in L-Dopa dose was significant for all drugs in relation to placebo, but was most significant for PRX and ENT ($p < 0.0001$). The most significant reduction in "off" duration was with PRG, PRX, and ENT ($p < 0.001$). The common tolerability measures were the percentage of patients withdrawn because of side effects, because of any reason, and because of the development of dyskinesias. Ropinirole, PRX, and ENT caused fewer withdrawals related to side effects. Pergolide was better than other analyzed drugs concerning withdrawals for any reason. All drugs caused more dyskinesias than placebo ($p < 0.0001$), with overlapping confidence intervals, except for TOL 600 mg, which caused more dyskinesias than dopamine agonists and ENT. Pramipexole and ENT had the best efficacy and tolerability profile in this analysis.

L9 ANSWER 82 OF 331 MEDLINE on STN DUPLICATE 61
ACCESSION NUMBER: 2000257785 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10796705
TITLE: Pergolide versus bromocriptine for levodopa-induced motor complications in Parkinson's disease.
AUTHOR: Clarke C E; Speller J M
CORPORATE SOURCE: Department of Neurology, City Hospital NHS Trust, Dudley Road, Birmingham, West Midlands, United Kingdom, B18 7QH.. c.e.clarke@bham.ac.uk
SOURCE: Cochrane database of systematic reviews (Online), (2000) No. 2, pp. CD000236. Ref: 4
Journal code: 100909747. E-ISSN: 1469-493X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 14 Jul 2000
Last Updated on STN: 14 Jul 2000
Entered Medline: 6 Jul 2000

AB OBJECTIVES: To compare the efficacy and safety of adjunct pergolide therapy versus bromocriptine in patients with Parkinson's disease, already established on levodopa and suffering the long-term complications of therapy. SEARCH STRATEGY: Electronic searches of MEDLINE, EMBASE and the Cochrane Controlled Trials Register. Handsearching of the neurology literature as part of the Cochrane Movement Disorders Group's strategy. Examination of the reference lists of identified studies and other reviews. Contact with Eli Lilly Company and Sandoz Limited. SELECTION CRITERIA: Randomised controlled trials of pergolide versus bromocriptine in patients with a clinical diagnosis of idiopathic Parkinson's disease and long-term complications of levodopa therapy. DATA COLLECTION AND ANALYSIS: Data was abstracted independently by each author and differences settled by discussion. MAIN RESULTS: Three short-term trials fulfilled the inclusion criteria for the review. Pergolide was superior to bromocriptine regarding UPDRS and NYPDS motor and NYPDS ADL scores in two trials. More patients recorded a 'marked' or 'moderate improvement' in clinician's global impression score with pergolide than bromocriptine in two studies. Insufficient evidence on fluctuations and dyskinesia was available to draw any conclusions. No significant differences between the agonists were seen in levodopa dose reduction, drop outs or adverse events. REVIEWER'S CONCLUSIONS: Although pergolide is superior to bromocriptine in reducing motor impairments and disability, no firm conclusions regarding levodopa-induced motor complications can be reached. Levodopa dose reduction, adverse events and withdrawals from treatment are similar for the two agonists. The small advantage of pergolide in efficacy does not take into account its additional cost compared with bromocriptine.

L9 ANSWER 83 OF 331 MEDLINE on STN DUPLICATE 62
ACCESSION NUMBER: 2000257784 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10796704
TITLE: Pergolide for levodopa-induced complications in Parkinson's disease.
AUTHOR: Clarke C E; Speller J M
CORPORATE SOURCE: Department of Neurology, City Hospital NHS Trust, Dudley Road, Birmingham, West Midlands, United Kingdom, B18 7QH.. c.e.clarke@bham.ac.uk
SOURCE: Cochrane database of systematic reviews (Online), (2000) No. 2, pp. CD000235. Ref: 1
Journal code: 100909747. E-ISSN: 1469-493X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 14 Jul 2000
Last Updated on STN: 14 Jul 2000
Entered Medline: 6 Jul 2000

AB OBJECTIVES: To compare the efficacy and safety of adjunct pergolide therapy versus placebo in patients with Parkinson's disease suffering from the complications of levodopa therapy. SEARCH STRATEGY: Electronic searches of MEDLINE, EMBASE and the Cochrane Controlled Trials Register. Handsearching of the neurology literature as part of the Cochrane Movement Disorders Group's strategy. Examination of the reference lists of identified studies and other reviews. Contact with Eli Lilly and Company Limited. SELECTION CRITERIA: Randomised controlled trials of pergolide versus placebo in patients with a clinical diagnosis of idiopathic Parkinson's disease and long-term complications of levodopa therapy. DATA COLLECTION AND ANALYSIS: Data was abstracted independently by each author and differences settled by discussion. The outcome measures used included Parkinson's disease rating scales, levodopa dosage, 'off' time measurements and the frequency of drop outs and adverse events. MAIN RESULTS: A large number of small RCTs were identified, but these were part of a large multicentre trial which was eventually published in full. The final publication was used as the only subject for this review. The time patients spent 'off' was reduced by 1.8 hours with pergolide compared with 0.2 hours with placebo ($p < 0.001$). Dyskinesia developed or deteriorated in 62% of pergolide-treated compared with 25% placebo-treated patients ($p < 0.05$). The excess in dyskinesia prevalence and severity resolved by the end of the study with levodopa reduction. Levodopa dose was reduced more in those receiving pergolide (235 mg v 51 mg; $p < 0.001$). Pergolide produced significant improvement in Hoehn and Yahr stage ($p < 0.05$) and both the motor and activities of daily living parts of a modified Columbia rating scale (both $p < 0.001$). Significantly more patients suffered nausea (24% v 13%; $p < 0.001$) and hallucinations (14% v 3%; $p < 0.01$) on pergolide. No difference was found in the numbers remaining on treatment at the end of the study (pergolide 84% v placebo 82%) but withdrawals due to adverse events were greater in those taking pergolide (10% v 4%). REVIEWER'S CONCLUSIONS: Based on this single large multicentre study, pergolide reduces 'off' time and improves impairment and disability due to Parkinson's disease whilst allowing a reduction in levodopa dose. This is at the expense of dopaminergic adverse events. Further trials are required to compare pergolide with the newer dopamine agonists.

L9 ANSWER 84 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 63

ACCESSION NUMBER: 2001:18468 BIOSIS
DOCUMENT NUMBER: PREV200100018468
TITLE: The dopamine agonist pramipexole scavenges hydroxyl free radicals induced by striatal application of 6-hydroxydopamine in rats: An in vivo microdialysis study.
AUTHOR(S): Ferger, Boris [Reprint author]; Teismann, Peter; Mierau, Joachim
CORPORATE SOURCE: Behavioural Neurobiology Laboratory, Swiss Federal Institute of Technology Zurich, Schorenstrasse 16, CH-8603, Schwerzenbach, Switzerland
ferger@toxi.biol.ethz.ch
SOURCE: Brain Research, (17 November, 2000) Vol. 883, No. 2, pp. 216-223. print.
CODEN: BRREAP. ISSN: 0006-8993.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Dec 2000
Last Updated on STN: 27 Dec 2000

AB Hydroxyl free radical production seems to play an important role in the pathogenesis of Parkinson's disease. In the present study, we investigated the dopamine agonists pramipexole and pergolide as well as the nitron compound S-PBN (N-tert-butyl-alpha-(2-sulphophenyl)nitron) to reduce hydroxyl radical formation. Microdialysis experiments were carried out in non-anaesthetized Wistar rats. Salicylate was incorporated into the perfusion fluid to measure indirectly hydroxyl radicals indicated by 2,3-dihydroxybenzoic acid (2,3-DHBA). Local perfusion with 0.2 or 2 nmol/2 µl/min 6-hydroxydopamine (6-OHDA) via the microdialysis probe significantly increased 2,3-DHBA levels 14-fold and 47-fold, respectively. Systemic application of either pergolide (0.05 mg/kg) or pramipexole (1 mg/kg) failed to significantly reduce 6-OHDA-induced hydroxyl radical production. In contrast, a 40 min pretreatment with pramipexole (2 and 10 nmol/2 µl/min via the probe) before onset of 6-OHDA perfusion, significantly attenuated 2,3-DHBA levels compared with vehicle controls. S-PBN pretreatment (2 nmol/2 µl/min) was not effective to reduce 2,3-DHBA levels. In conclusion, pramipexole was able to reduce hydroxyl radical levels induced by 6-OHDA in vivo after local application. This property of pramipexole may be beneficial under conditions of enhanced hydroxyl radical formation in parkinsonian brains and may add to its well known dopamine D2-like receptor agonistic effects.

L9 ANSWER 85 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 64

ACCESSION NUMBER: 2001:56832 BIOSIS
DOCUMENT NUMBER: PREV200100056832
TITLE: Antisaccadic effects of a dopamine agonist as add-on therapy in advanced Parkinson's patients.
AUTHOR(S): Crevits, Luc [Reprint author]; Versijpt, Jan; Hanse, Monique; De Ridder, Katrien
CORPORATE SOURCE: Department of Neurology, Oto-Neuro-Ophthalmology Unit, University Hospital, De Pintelaan 185, B-9000, Ghent, Belgium
luc.crevits@rug.ac.be
SOURCE: Neuropsychobiology, (November, 2000) Vol. 42, No. 4, pp. 202-206. print.
CODEN: NPBIAL. ISSN: 0302-282X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jan 2001
Last Updated on STN: 12 Feb 2002

AB We wanted to compare clinical neurological and antisaccadic behavior before and after addition of a dopamine agonist to the usual antiparkinsonian drugs in advanced Parkinson's disease. Parkinson's patients in stage 3 and 4 of Hoehn and Yahr not yet taking a dopamine agonist were selected. In 20 patients, the treating neurologist decided to add pergolide. The dose of pergolide was adjusted by the treating neurologist according to clinical response. Antisaccades were studied by infrared oculography before and after addition of pergolide. Antisaccades are voluntary saccades in the opposite direction of an unanticipated visual target. The patients made more errors, i.e. they glanced to the target or they made no eye movement at all. In contradistinction to the global neurological improvement and the better motor scores, antisaccadic disturbances did not improve significantly with pergolide, except in younger patients. These findings suggest that antisaccadic alterations in patients with advanced Parkinson's disease could

be multifaceted. Not only depletion of dopamine, but also non-dopaminergic dysfunctions could contribute. Cortical frontal lesions must also be taken into account.

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ACCESSION NUMBER: 2001128095 EMBASE
TITLE: Pergolide and Parkinson's disease.
SOURCE: Prescrire International, (2000) Vol. 9, No. 50, pp. 177-179.
Refs: 28
ISSN: 1167-7422 CODEN: PRINFU
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Apr 2001
Last Updated on STN: 19 Apr 2001

AB Levodopa is the cornerstone of therapy for Parkinson's disease, and bromocriptine is the reference drug for patients who develop motor complications on levodopa. Pergolide, a dopamine agonist, is now marketed in France for the treatment of motor complications associated with levodopa therapy. Four trials comparing pergolide with bromocriptine have been published. The methodological quality of these trials varies, and their published reports often lack details. Taken together, these trials fail to demonstrate that pergolide provides a tangible clinical advantage over bromocriptine. Pergolide has not been compared with other dopamine agonists in double-blind trials. Pergolide has the same safety profile as other dopamine agonists.

L9 ANSWER 87 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:175939 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 38-11382
TITLE: Pergolide and Parkinson's disease: no clear benefit
AUTHOR(S): anon
SOURCE: Prescrire International (France), (Dec 2000) Vol. 9, pp. 177-179. 28 Refs.
ISSN: 1167-7422.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 2001:11382
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB An overview of clinical studies on the use of pergolide (Celance) for Parkinson disease and comparison of pergolide to other antiparkinson agents such as levodopa and bromocriptine is presented; data on neurological and GI adverse effects and drug interactions are presented.
B. V. Borders-Hemphill

L9 ANSWER 88 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 66

ACCESSION NUMBER: 2001:261686 BIOSIS
DOCUMENT NUMBER: PREV200100261686
TITLE: Iron chelating, antioxidant and cytoprotective properties

of dopamine receptor agonist; apomorphine.
AUTHOR(S): Youdim, M. B. H. [Reprint author]; Gassen, M.; Gross, A.;
Mandel, S.; Grunblatt, E.
CORPORATE SOURCE: Department of Pharmacology, Faculty of Medicine, Eve Topf
and National Parkinson's Foundation Centers, Technion,
Haifa, Israel
youdim@tx.technion.ac.il
SOURCE: Journal of Neural Transmission Supplement, (2000)
Vol. 58, pp. 83-96. print.
CODEN: JNTSD4. ISSN: 0303-6995.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 30 May 2001
Last Updated on STN: 19 Feb 2002

AB There have been many attempts to discover neuroprotective drugs for the
treatment of Parkinson's disease (PD). Many of these compounds
either do not cross the blood brain barrier or are not very effective in
the 6-hydroxydopamine or MPTP (N-methyl-4-phenyl-1,2,3,6-
tetrahydropyridine) models of PD. We have examined several compounds
including dopamine receptor agonist bromocriptine, lisuride,
pergolide and R-apomorphine for their neuroprotective action
against the above neurotoxins in PC12 and dopamine neuroblastoma cell
lines in culture and in vivo. R-apomorphine exhibited relatively potent
neuroprotective action in vitro, cell culture and in vivo as a radical
scavenger and iron chelator, because of its catechol structure. The
recent clinical trials with apomorphine, where parkinsonian
subjects can be weaned off L-dopa would suggest that this drug either
exerts a neuroprotective action or that continuous sustained stimulation
of dopamine receptor may be responsible for its unusual pharmacological
activity. Apomorphine has a far more broad neuroprotective activity in
the various models as compared with l-selegiline and may therefore be an
ideal drug to study neuroprotection in parkinsonian subjects
with the use of PET or SPECT.

L9 ANSWER 89 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 67
ACCESSION NUMBER: 2001:49017 CAPLUS
DOCUMENT NUMBER: 135:86375
TITLE: Iron chelating, antioxidant and cytoprotective
properties of dopamine receptor agonist; apomorphine
AUTHOR(S): Youdim, M. B. H.; Gassen, M.; Gross, A.; Mandel, S.;
Grunblatt, E.
CORPORATE SOURCE: Department of Pharmacology, Eve Topf and National
Parkinson's Foundation Centers, Bruce Rappaport Family
Research Institute, Faculty of Medicine, Haifa, Israel
SOURCE: Advances in Research on Neurodegeneration (2000), 7(7th International Winter Conference
on Neurodegeneration, 1999), 83-96
CODEN: ARNEFX; ISSN: 1068-719X
PUBLISHER: Springer-Verlag Wien
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 30 refs. There have been many attempts to discover
neuroprotective drugs for the treatment of Parkinson's disease
(PD). Many of these compds. either do not cross the blood brain barrier
or are not very effective in the 6-hydroxydopamine or MPTP
(N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) models of PD. We have
examined several compds. including dopamine receptor agonist bromocriptine,
lisuride, pergolide and R-apomorphine for their neuroprotective
action against the above neurotoxins in PC12 and dopamine neuroblastoma
cell lines in culture and in vivo. R-apomorphine exhibited relatively
potent neuroprotective action in vitro, cell culture and in vivo as a
radical scavenger and iron chelator, because of its catechol structure.

The recent clin. trials with apomorphine, where parkinsonian subjects can be weaned off L-dopa would suggest that this drug either exerts a neuroprotective action or that continuous sustained stimulation of dopamine receptor may be responsible for its unusual pharmacol. activity. Apomorphine has a far more broad neuroprotective activity in the various models as compared with 1-selegiline and may therefore be an ideal drug to study neuroprotection in parkinsonian subjects with the use of PET or SPECT.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 90 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 68

ACCESSION NUMBER: 2000:92856 CAPLUS

DOCUMENT NUMBER: 132:117010

TITLE: Comparative tolerability of the newer generation antiparkinsonian agents

AUTHOR(S): Lambert, Dorothee; Waters, Cheryl H.

CORPORATE SOURCE: Department of Neurology, Division of Movement Disorders, University of Southern California, Los Angeles, CA, USA

SOURCE: Drugs & Aging (2000), 16(1), 55-65

CODEN: DRAGE6; ISSN: 1170-229X

PUBLISHER: Adis International Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 44 refs. In recent years, the treatment of Parkinson's disease has undergone an immense amount of research, resulting in the development of multiple new medications. This has largely been fuelled by dissatisfaction over the development of motor complications secondary to long term levodopa therapy. Different treatment approaches are applied depending on the stage of Parkinson's disease. In early and mild Parkinson's disease, selegiline offers a limited symptomatic effect. Its neuroprotective effect, although at present theor., has questionable clin. relevance. Increased mortality associated with selegiline has been reported, although a meta-anal. of 5 different trials did not support this finding. The newer, non-ergoline dopamine agonists, pramipexole and ropinirole, have undergone extensive studies to evaluate their efficacy as monotherapy in early Parkinson's disease. These newer agonists are ideal initial symptomatic medications, primarily because they delay the onset of levodopa-induced motor fluctuations. Efficacy of the newer dopamine agonists in advanced disease seems to be comparable to that of the older agents, bromocriptine and pergolide. Adverse effects can be reduced by starting the medication at a very low dose and then slowly titrating upward. Catechol-O-Me transferase (COMT) inhibitors are indicated for the treatment of motor fluctuations in advanced disease, particularly the "wearing-off" phenomenon. Tolcapone, a peripheral and central COMT inhibitor, appears to be quite effective, producing a 47% reduction in "off" time. Unfortunately, 3 deaths have been observed, which are presumably secondary to tolcapone therapy. The drug has been withdrawn in many countries, and liver enzyme testing is mandatory in the US. Entacapone, a purely peripheral COMT inhibitor with a lower potency than tolcapone, has also proved to be effective and has not been associated with liver damage, obviating the need for testing.

OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 91 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights

ACCESSION NUMBER: 2000344694 EMBASE
TITLE: Dopamine agonists: The treatment for Parkinson's disease in the XXI century?.
AUTHOR: Lledo, A. (correspondence)
CORPORATE SOURCE: Lilly Research Centre (CNS), Erl Wood Manor, Sunninghill Rd., S., Windlesham, United Kingdom. lledo_alberto@lilly.com
AUTHOR: Lledo, A. (correspondence)
CORPORATE SOURCE: Lilly Research Centre, CNS, Erl Wood Manor, Sunninghill Road, Windlesham, Surrey GU20 6PH, United Kingdom.
SOURCE: Parkinsonism and Related Disorders, (Nov 2000)
Vol. 7, No. 1, pp. 51-58.
Refs: 57
ISSN: 1353-8020 CODEN: PRDIFO
PUBLISHER IDENT.: S 1353-8020(00)00038-9
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 27 Nov 2000
Last Updated on STN: 27 Nov 2000

AB Levodopa combined with a peripheral dopa-decarboxylase inhibitor (DCI) has been considered the therapy of choice for Parkinson's disease (PD). Levodopa is nearly always effective, but has a high incidence of adverse effects with long term use, including response fluctuations (on/off phenomena) and dyskinesias. Dopaminergic agonists, acting directly at the receptor level, would be able to decrease the incidence of these motor complications. In progressive neurodegenerative diseases, such as PD, modification of the rate of disease progression (often referred to as neuroprotection) is currently a highly debated topic. Increased oxidative stress is thought to be involved in nigral cell death, that is characteristic of PD. This oxidative stress may be further exacerbated by levodopa therapy. These mechanisms have been proven in vitro and animal models, but it's relevance in humans remains speculative. Based on the considerations above, the emerging therapeutic strategies for PD advocate early use of dopamine agonists in the treatment of PD. A number of recent well-controlled studies have proven the efficacy of dopamine agonists used as monotherapy. Moreover, as predicted by animal studies, on the long term, dopaminergic agonists induce significantly less motor complications than levodopa. In the last 2 years, three new dopamine agonists have been launched, including ropinirole, pramipexole and cabergoline. These new agonists have been added, as therapeutical options to well-established drugs, like pergolide, bromocriptine or talipexole. The recently launched compounds have proven efficacy in monotherapy and as adjunctive therapy to levodopa. Unfortunately, only a very limited amount of comparative data among the different agonists is available. Pergolide has proven to be a superior drug to bromocriptine as adjunctive therapy to levodopa in a significant number of studies and is considered the gold standard dopamine agonist. Nevertheless, none of the recently launched compounds has compared itself against pergolide. A comparison of monotherapy trials is difficult, because of differences in design and populations. In a recently completed trial pergolide was statistically significantly better than placebo in all the efficacy parameters tested, with 57% of pergolide treated patients improving over 30% in the motor section of the UPDRS, as compared to 17% in the placebo arm. Interestingly, these results were obtained in the absence of any other antiparkinsonian drug during the trial. Recent monotherapy trials

done with ropinirole and pramipexole achieved also significant improvements as monotherapy, but in these cases selegeline, a drug that causes a symptomatic improvement in PD, was allowed as co-medications during the trial. Not all trials used the same efficacy measures, i.e. monotherapy trials with pergolide and ropinirole used a 'responder' based analysis (responder were all patients that improved 30% or more on the motor section of UPDRS), as well as a baseline to endpoint improvement in motor scores. Pramipexole monotherapy trials used only the latter approach, which is clinically less powerful than a responder analysis. Even with the difficulties mentioned above, all the recent trials with dopamine agonists have proven that these drugs are a useful symptomatic long term treatment for PD with or without levodopa and that the early use of dopamine agonists reduces the incidence of motor complications as compared to levodopa. (C) 2000 Elsevier Science Ltd.

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STN DUPLICATE 70

ACCESSION NUMBER: 2000:460404 BIOSIS
DOCUMENT NUMBER: PREV200000460404
TITLE: Parkinson's disease and sleep.
AUTHOR(S): Clarenbach, P. [Reprint author]
CORPORATE SOURCE: Dept. of Neurology, Ev. Johannes-Hospital, Bielefeld, Germany
SOURCE: Journal of Neurology, (September, 2000) Vol. 247, No. Suppl. 4, pp. 20-23. print.
CODEN: JNRYA9. ISSN: 0340-5354.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Oct 2000
Last Updated on STN: 10 Jan 2002

AB There are many reasons for patients with idiopathic Parkinson's disease to develop sleep disorders and subsequent daytime sleepiness. Important causes are reduction of total sleep duration and sleep efficiency, and an increase in respiratory and motor arousals. This daytime sleepiness at first glance seems different from the "sleep attacks" which caused motor vehicle mishaps reported recently in persons taking pramipexole and ropinirole. There is, however, only little evidence that we deal with a new phenomenon in a new clinical situation, i. e. cataplexy-like attacks after high doses of new non-ergot dopamine-agonists. Until now there is no single case of a proven cataplexy on one hand, and older dopamine agonists like pergolide as well as L-Dopa + carbidopa have been reported to induce sudden onsets of sleep, too.

L9 ANSWER 93 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 71

ACCESSION NUMBER: 2000:460403 BIOSIS
DOCUMENT NUMBER: PREV200000460403
TITLE: Long-term treatment with dopamine agonists in idiopathic Parkinson's disease.
AUTHOR(S): Reichmann, H. [Reprint author]
CORPORATE SOURCE: Dept. of Neurology, University of Dresden, Fetscherstrasse 74, 01307, Dresden, Germany
SOURCE: Journal of Neurology, (September, 2000) Vol. 247, No. Suppl. 4, pp. 17-19. print.
CODEN: JNRYA9. ISSN: 0340-5354.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Oct 2000
Last Updated on STN: 10 Jan 2002

AB Long-term treatment studies with any antiparkinsonian drug are rather limited. Especially, double-blind, randomized and multi-center

studies do not exist except for some rare exceptions. Nonetheless, such studies are mandatory to prove certain therapy regimens. This overview reports on the comparison between dopamine agonists and levodopa. There are open studies comparing bromocriptine, lisuride, pergolide with levodopa which demonstrate that the use of dopamine agonists in monotherapy or combination with levodopa decreases the percentage of patients who develop dyskinesias compared to levodopa only. A long-term study was performed with cabergoline (3 years) which was extended in an open trial for another 2 years and which underlined the above mentioned observation. In a very recent study, ropinirole was compared with levodopa. This double-blind study spans 5 years and shows that about 30 % of patients were able to stay for 5 years on ropinirole monotherapy, that withdrawal rate was not higher in the dopamine agonist group and that the side effects were similar in the levodopa and the ropinirole group. The major finding of this study was a very low dyskinesia rate when treating patients with ropinirol alone. Thus, this study underlines our therapy concept which advocates the early use of dopamine agonists in IPS.

L9 ANSWER 94 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:1764 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 37-07423
TITLE: Clinical pharmacology of dopamine agonists
AUTHOR(S): Lam, Y. W.
CORPORATE SOURCE: Dept. of Pharmacol., Univ. of Texas Hlth. Sci. Ctr., 7703
Floyd Curl Dr., San Antonio, TX 78284-6220, USA
SOURCE: Pharmacotherapy (USA), (2000) Vol. 20, pp.
17S-25S, 43S-46S. 57 Refs.
CODEN: PHPYDQ. ISSN: 0277-0008.
DOCUMENT TYPE: General Review
FILE SEGMENT: IPA
OTHER SOURCE: IPA 2000:7423
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB A review of the use of dopamine agonists, including bromocriptine, cabergoline, pergolide, apomorphine, pramipexole, and ropinirole, in the treatment of Parkinson's disease is presented, and dopamine receptors, the role of dopamine agonists in Parkinson's disease, the pharmacokinetics, neuroendocrine effects, adverse effects, and drug interactions of these agents, and the clinical efficacy of pramipexole, ropinirole, and cabergoline are considered. This article is one in a series of 5 that together qualify for 2 hours U.S. CE credit by the ACPE.
Ramune T. Dailide

L9 ANSWER 95 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 72

ACCESSION NUMBER: 2000:542644 BIOSIS
DOCUMENT NUMBER: PREV200000542644
TITLE: Pre-clinical studies of pramipexole: Clinical relevance.
AUTHOR(S): Hubble, J. P. [Reprint author]
CORPORATE SOURCE: Department of Neurology, The Ohio State University
Parkinson's Disease Center, 1581 Dodd Drive, Suite 371,
Columbus, OH, 43210, USA
SOURCE: European Journal of Neurology, (May, 2000) Vol.
7, No. Supplement 1, pp. 15-20. print.
ISSN: 1351-5101.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 2000
Last Updated on STN: 11 Jan 2002

AB This paper reviews the preclinical study of the novel dopamine agonist pramipexole and its use in early Parkinson's disease (PD). Emphasis will be given to those properties distinguishing this drug from other dopamine agonists, the relevance of the preclinical data to clinical trial results in early PD, and the putative neuroprotective properties of the compound. The conventional dopamine agonists are ergot-derived compounds that are most widely used as adjunctive therapies in advancing Parkinson's disease (PD). Examples of conventional agonists are bromocriptine and pergolide. Pramipexole is an aminobenzothiazole compound, recently introduced for the treatment of both early and advanced PD. Its nonergot structure may reduce the risk of side-effects, considered unique to ergot drugs, such as membranous fibrosis. Pramipexole is a full dopamine agonist with high selectivity for the D2 dopamine receptor family. This family includes the D2, D3 and D4 receptor subtypes. Pramipexole has a 5- to 7-fold greater affinity for the D3 receptor subtype with lower affinities for the D2 and D4 receptor subtypes. The drug has only minimal alpha2-adrenoceptor activity and virtually no other receptor agonism or antagonism. The optimal dopamine receptor activation for the safe and effective treatment of PD is not known. Findings in animal models and clinical studies indicate that activation of the postsynaptic D2 receptor subtype provides the most robust symptomatic improvement in PD. Given its pharmacological profile, it is not surprising that pramipexole was found to be effective in ameliorating parkinsonian signs in animal models. This therapeutic effect has been confirmed in clinical trials in both early and advanced PD. In early disease, it provides a clear reduction in the chief motor manifestations of PD and improved activities of daily living. Perhaps most striking is the large number of clinical trial patients who have remained on pramipexole monotherapy for many months. The majority of these subjects have been maintained on pramipexole for an excess of 24 months without requiring additional symptomatic treatment with levodopa. This is in contrast to the general clinical experience with older conventional agonists. Pramipexole also has a favourable pharmacokinetic profile. It is rapidly absorbed with peak levels appearing in the bloodstream within 2 h of oral dosing. It has a high absolute bioavailability of > 90% and can be administered without regard to meals. It has no significant effects on other antiparkinson drugs such as levodopa or selegiline. Its excretion is primarily renal and, thus, has little or no impact on hepatic cytochrome P450 enzymes or other related metabolic pathways. Pramipexole has also been theorized to have 'neuroprotectant' properties. Oxyradical generation is posited as a cause or accelerant of brain nigral cell death in PD. Pramipexole stimulates brain dopamine autoreceptors and reduces dopamine synthesis and turnover which may minimize oxidative stress due to dopamine metabolism. Furthermore, the compound has a low oxidation potential that may serve as an oxyradical scavenger in the PD brain. In summary, pramipexole is a new antiparkinson medication found to have unique dopamine agonist characteristics and putative neuroprotective properties.

L9 ANSWER 96 OF 331 MEDLINE on STN
ACCESSION NUMBER: 2001118262 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11199812
TITLE: Parkinson's disease and sleep.
AUTHOR: Clarenbach P
CORPORATE SOURCE: Dept. of Neurology, Ev. Johannes-Hospital. Bielefeld, Germany.
SOURCE: Journal of neurology, (2000 Sep) Vol. 247 Suppl 4, pp. IV/20-3. Ref: 21
Journal code: 0423161. ISSN: 0340-5354.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 15 Feb 2001

AB There are many reasons for patients with idiopathic Parkinson's disease to develop sleep disorders and subsequent daytime sleepiness. Important causes are reduction of total sleep duration and sleep efficiency, and an increase in respiratory and motor arousals. This daytime sleepiness at first glance seems different from the "sleep attacks" which caused motor vehicle mishaps reported recently in persons taking pramipexole and ropinirole. There is, however, only little evidence that we deal with a new phenomenon in a new clinical situation, i. e. cataplexy-like attacks after high doses of new non-ergot dopamine-agonists. Until now there is no single case of a proven cataplexy on one hand, and older dopamine agonists like pergolide as well as L-Dopa + carbidopa have been reported to induce sudden onsets of sleep, too.

L9 ANSWER 97 OF 331 MEDLINE on STN
ACCESSION NUMBER: 2001118260 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11199810
TITLE: Long-term treatment with dopamine agonists in idiopathic Parkinson's disease.
AUTHOR: Reichmann H
CORPORATE SOURCE: Dept of Neurology, University of Dresden, Germany.
SOURCE: Journal of neurology, (2000 Sep) Vol. 247 Suppl 4, pp. IV/17-9. Ref: 10
Journal code: 0423161. ISSN: 0340-5354.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 15 Feb 2001

AB Long-term treatment studies with any antiparkinsonian drug are rather limited. Especially, double-blind, randomized and multicenter studies do not exist except for some rare exceptions. Nonetheless, such studies are mandatory to prove certain therapy regimens. This overview reports on the comparison between dopamine agonists and levodopa. There are open studies comparing bromocriptine, lisuride, pergolide with levodopa which demonstrate that the use of dopamine agonists in monotherapy or combination with levodopa decreases the percentage of patients who develop dyskinesias compared to levodopa only. A long-term study was performed with cabergoline (3 years) which was extended in an open trial for another 2 years and which underlined the above mentioned observation. In a very recent study, ropinirole was compared with levodopa. This double-blind study spans 5 years and shows that about 30% of patients were able to stay for 5 years on ropinirole monotherapy, that withdrawal rate was not higher in the dopamine agonist group and that the side effects were similar in the levodopa and the ropinirole group. The major finding of this study was a very low dyskinesia rate when treating patients with ropinirol alone. Thus, this study underlines our therapy concept which advocates the early use of dopamine agonists in IPS.

L9 ANSWER 98 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 73
ACCESSION NUMBER: 2000:29987 CAPLUS
DOCUMENT NUMBER: 132:58680

TITLE: Treatment of Parkinson's disease with ropinirole after
pergolide-induced retroperitoneal fibrosis
AUTHOR(S): Lund, Brian C.; Neiman, Richard F.; Perry, Paul J.
CORPORATE SOURCE: College of Pharmacy, University of Iowa, Iowa City,
IA, 52242-1112, USA
SOURCE: Pharmacotherapy (1999), 19(12), 1437-1444
CODEN: PHPYDQ; ISSN: 0277-0008
PUBLISHER: Pharmacotherapy Publications
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pergolide is a dopaminergic agonist used to treat
Parkinson's disease but is associated with the development of
retroperitoneal fibrosis (RPF). Newer nonergot agents (pramipexole,
ropinirole) may not carry this same risk. A patient with a history of
pergolide-induced RPF was treated successfully with ropinirole for
1 yr without complications.
OS.CITING REF COUNT: 12 THERE ARE 12 CAPLUS RECORDS THAT CITE THIS
RECORD (12 CITINGS)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 99 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:1415 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 37-06105
TITLE: Treatment of Parkinson's disease with ropinirole after
pergolide-induced retroperitoneal fibrosis
AUTHOR(S): Lund, B. C.; Neiman, R. F.; Perry, P. J.
CORPORATE SOURCE: Univ. of Iowa, Coll. of Pharm., 443 S. Pharm. Bldg., Iowa
City, IA 52242-1112, USA
SOURCE: Pharmacotherapy (USA), (1999) Vol. 19, pp.
1437-1438. 15 Refs.
CODEN: PHPYDQ. ISSN: 0277-0008.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 2000:6105
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001
AB The case of an 83-yr-old woman with Parkinson's disease and a
history of retroperitoneal fibrosis caused by 3 mg/day pergolide
who was successfully treated with 1.5 mg/day ropinirole without
complications is described.
Ellen Katz Neumann

L9 ANSWER 100 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:949 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 37-04059
TITLE: Vitiligo associated with tolcapone and levodopa in a
patient with Parkinson's disease
AUTHOR(S): Sabate, M.; Bosch, A.; Pedros, C.; Figueras, A.
CORPORATE SOURCE: Serv. de Farmacologia Clin., Unitat de Farmacologia, Univ.
Autonoma de Barcelona, CSU Vall d'Hebron, E-08035
Barcelona, Spain Internet: afs@icf.uab
SOURCE: Annals of Pharmacotherapy, (Nov 1999) Vol. 33,
pp. 1228-1229. 5 Refs.
CODEN: APHRER. ISSN: 1060-0280.
DOCUMENT TYPE: Letter
FILE SEGMENT: IPA
OTHER SOURCE: IPA 2000:4059
LANGUAGE: English

ENTRY DATE: Entered STN: 16 Nov 2001

Last Updated on STN: 16 Nov 2001

AB The case of a 50-yr-old man with Parkinson's disease who developed vitiligo associated with 300 mg/day tolcapone and 375 mg/day levodopa is described. Concomitant therapy included carbidopa and pergolide. The vitiligo started 1 wk after tolcapone was added to the regimen. Due to worsening of the condition, bilateral pallidotomy was performed; however, drug therapy was continued. In the months following pallidotomy, his skin lesions continued to enlarge.
Ellen Katz Neumann

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STN DUPLICATE 74

ACCESSION NUMBER: 1999:230306 BIOSIS

DOCUMENT NUMBER: PREV199900230306

TITLE: Switching dopamine agonists in advanced Parkinson's disease: Is rapid titration preferable to slow?.

AUTHOR(S): Goetz, Christopher G. [Reprint author]; Blasucci, Lucy; Stebbins, Glenn T.

CORPORATE SOURCE: Department of Neurological Sciences, Rush University/Rush-Presbyterian-St. Luke's Medical Center, 1725 W. Harrison St., Chicago, IL, 60612, USA

SOURCE: Neurology, (April 12, 1999) Vol. 52, No. 6, pp. 1227-1229. print.

CODEN: NEURAI. ISSN: 0028-3878.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 17 Jun 1999

Last Updated on STN: 17 Jun 1999

AB Background: New dopamine agonists are available, but no study has examined safe and effective ways to switch from one agonist to another. Objective: To compare rapid- versus slow-titration schedules for starting a new dopamine agonist in patients already on chronic agonist therapy for Parkinson's disease. Methods: Sixteen patients on stable carbidopa/levodopa and a dopamine agonist (bromocriptine or pergolide) switched to pramipexole using a conversion calculation of 1:1 for pergolide dose and 10:1 for bromocriptine dose. Patients were randomized to two titration schedules-either slow titration, following the package insert and taking up to 8 weeks to reach their equivalent dosage (8 patients), or rapid titration, receiving the full converted dose the day after stopping the former agonist (8 patients) with subsequent weekly dose adjustments. Using a blinded observer, the primary outcome variable was the time required to a Unified Parkinson's Disease Rating Scale (UPDRS) motor score superior to baseline without increased adverse effects. Results: Both groups showed equivalent and statistically significant improvement after switching to the new agonist. The mean time to reach a UPDRS score that was superior to baseline without increased adverse effects was significantly shorter in the rapid-titration group (mean 2.1 weeks versus 5.3 weeks). Furthermore, with slow titration two patients experienced enhanced parkinsonian serious adverse effects requiring hospitalization (two falls with fractures). Conclusion: The switchover from one agonist to another can be safely and successfully accomplished with a rapid titration based on an equivalency dose calculation.

L9 ANSWER 102 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 75

ACCESSION NUMBER: 1999400546 EMBASE

TITLE: The effect of dopamine agonist therapy on dopamine transporter imaging in Parkinson's disease.

AUTHOR: Ahlskog, J. Eric, Dr. (correspondence); Maraganore, Demetrius M.; Matsumoto, Joseph Y.; Stark, Kathy F.

CORPORATE SOURCE: Department of Neurology, Mayo Clinic, Rochester, MN, United States.

AUTHOR: O'Connor, Michael K.

CORPORATE SOURCE: Department of Nuclear Medicine, Mayo Clinic, Rochester, MN, United States.

AUTHOR: Ahlskog, J. Eric, Dr. (correspondence)

CORPORATE SOURCE: Dept. of Neurology, Mayo Clinic, Rochester, MN 55905, United States.

AUTHOR: Uitti, Ryan J.; Turk, Margaret F.; Burnett, Omer L.

SOURCE: Movement Disorders, (1999) Vol. 14, No. 6, pp. 940-946.
Refs: 25
ISSN: 0885-3185 CODEN: MOVDEA

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 014 Radiology
023 Nuclear Medicine
037 Drug Literature Index
008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 2 Dec 1999
Last Updated on STN: 2 Dec 1999

AB Single-photon emission computed tomography (SPECT) imaging with the dopamine transporter ligand, [(123)I] β -CIT (2 β -carboxymethoxy-3 β -[4-iodophenyl] tropane), has been proposed as a means of measuring Parkinson's disease (PD) progression. To be useful in this role, however, [(123)I] β -CIT imaging should not be influenced by the medications used to treat PD, including the dopamine agonist drugs such as pergolide. We assessed the effect of adjunctive pergolide administration on [(123)I] β -CIT uptake in 12 patients with PD, who were being treated with levodopa, initiating pergolide therapy for motor fluctuations. Patients underwent [(123)I] β -CIT imaging at baseline, subsequently while on pergolide therapy (6 weeks), and again 4 weeks after pergolide wash-out. Uptake in the striatum was averaged for the two sides and expressed as (striatum - occipital)/occipital, with similar calculations for putamen and caudate. Consistent with PD, the patients' mean striatal and putamen uptake ratios at baseline were significantly less ($p < 0.001$) than the mean values from 26 normal control subjects of similar age. During pergolide treatment, the striatal and putamen [(123)I] β -CIT uptake ratios were each statistically similar to baseline, although there was a slight trend toward an increased striatal value (8% higher on pergolide; $p = 0.105$). Caudate [(123)I] β -CIT uptake was 11% higher on pergolide therapy (nominal $p = 0.042$, but not significant when adjusted for multiple comparisons: $p = 0.126$). After pergolide washout, the striatal, putamen, and caudate uptake ratios did not differ from baseline. Therefore, we found that pergolide therapy did not significantly affect [(123)I] β -CIT SPECT imaging but we cannot exclude a small influence.

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ACCESSION NUMBER: 2000:22367 BIOSIS

DOCUMENT NUMBER: PREV200000022367

TITLE: An overnight switch to ropinirole therapy in patients with Parkinson's disease: Short communication.

AUTHOR(S): Canesi, M.; Antonini, A.; Mariani, C. B.; Tesei, S.; Zecchinelli, A. L.; Barichella, M.; Pezzoli, G. [Reprint author]

CORPORATE SOURCE: Department of Neuroscience, Parkinson Institute Milan,

Istituti Clinici di Perfezionamento, Via Bignami 1,
I-20126, Milano, Italy

SOURCE: Journal of Neural Transmission, (1999) Vol. 106,
No. 9-10, pp. 925-929. print.
CODEN: JNGSE8. ISSN: 0300-9564.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 29 Dec 1999
Last Updated on STN: 31 Dec 2001

AB Patients with Parkinson's disease (n = 68) switched from
pergolide or bromocriptine to ropinirole overnight (dose
equivalence ratios - 1:6 and 10:6, respectively). The activities of daily
living score for the Unified Parkinson's Disease Rating Scale
(UPDRS) was significantly improved 4 weeks after the
bromocriptine-ropinirole switch. All other UPDRS scores, including that
for the side-effect component, were not significantly different after
either switch. Overnight switching may be a safe therapeutic approach
that may reduce hospitalisation and related socio-economic costs.

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ACCESSION NUMBER: 1999378198 EMBASE

TITLE: Treatment of Parkinson's disease should begin with a
dopamine agonist.

AUTHOR: Montastruc, Jean Louis, Dr. (correspondence); Rascol,
Olivier; Senard, Jean-Michel

CORPORATE SOURCE: Lab. de Pharmacologie Med. et Clin., Inserm U 317, Hopitaux
de Toulouse, Toulouse, France.

AUTHOR: Montastruc, Jean Louis, Dr. (correspondence)

CORPORATE SOURCE: Lab. de Pharmacologie Med. et Clin., Faculte de Medecine,
37 allees Jules-Guesde, 31073 Toulouse Cedex, France.

AUTHOR: Montastruc, Jean Louis, Dr. (correspondence)

CORPORATE SOURCE: Lab. Pharmacologie Medicale Clinique, Faculte de Medecine,
37 allees Jules-Guesde, 31073 Toulouse Cedex, France.

SOURCE: Movement Disorders, (1999) Vol. 14, No. 5, pp.
725-730.
Refs: 49
ISSN: 0885-3185 CODEN: MOVDEA

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 18 Nov 1999
Last Updated on STN: 18 Nov 1999

AB The occurrence of side effects with lone-term levodopa therapy, such as
fluctuations in motor performance or abnormal movements, led to a search
for new antiparkinsonian drugs. Dopamine agonists include ergot
derivatives such as bromocriptine, lisuride, pergolide, and
cabergoline and other agents which do not possess the ergot structure such
as pramipexole and ropinirole. They all are powerful stimulators of the
D2 dopamine receptor which probably underlies their therapeutic effects.
The clinical consequences of their binding to other dopamine receptor
subtypes (D1 or D3) remains unknown. They are usually prescribed in
combination with levodopa when late side effects begin to occur. This
review summarizes the available pharmacologic and clinical data to support
the early use of dopamine agonists in Parkinson's disease.
Several strategies can be used, such as monotherapy or 'early' or 'late'
combination with levodopa. Results of recent well-performed, modern

clinical trials show that early use of the new dopamine agonists is able to effectively control the clinical symptoms for more than 3 years thereby offering the possibility of delaying the occurrence of levodopa-induced late motor side effects.

L9 ANSWER 105 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 78
ACCESSION NUMBER: 1999:573101 CAPLUS
DOCUMENT NUMBER: 131:208984
TITLE: Pergolide monotherapy in the treatment of early PD: a randomized, controlled study
AUTHOR(S): Barone, P.; Bravi, D.; Bermejo-Pareja, F.; Marconi, R.; Kulisevsky, J.; Malagu, S.; Weiser, R.; Rost, N.; Bracco, F.; Abbruzzese, G.; Marchese, R.; Cazzato, G.; Capus, L.; Di Perri, R.; Morgante, L.; Epifanio, A.; Ferrari, E.; Lamberti, P.; Piccoli, F.; Rizza, L.; Rasi, F.; Saquegna, T.; Scarpino, O.; Guidi, M.; Tonali, P.; Albanese, A.; Quattrone, A.; Zappia, M.; Filla, A.; Pellecchia, M. T.; Calzetti, S.; Negrotti, A.; Molina, J. A.; Martinez-Martin, P.; Balseiro, J.; Pascual, B.; Steiger, M.; Lledo, A.; Quail, D.; Williamson, D.; Gomez, J. C.
CORPORATE SOURCE: The Pergolide Monotherapy Study Group, Department of Neurological Sciences, University of Napoli, Naples, 80131, Italy
SOURCE: Neurology (1999), 53(3), 573-579
CODEN: NEURAI; ISSN: 0028-3878
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The efficacy and tolerability of pergolide in patients with idiopathic Parkinson's disease (PD) were evaluated in a multicenter, double-blind, randomized, parallel-group, 3-mo trial vs. placebo. By the end of the study, the mean dose of pergolide was 2.06 mg/day. Six patients in the pergolide group vs. 2 patients in the placebo group discontinued the study because of treatment emergent side effects. The good clin. responses suggest that pergolide monotherapy may be an effective and well-tolerated 1st-line treatment in patients with early-stage PD.

OS.CITING REF COUNT: 40 THERE ARE 40 CAPLUS RECORDS THAT CITE THIS RECORD (41 CITINGS)
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 106 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 79
ACCESSION NUMBER: 2000:39840 CAPLUS
DOCUMENT NUMBER: 132:73114
TITLE: Cabergoline: a review of its efficacy in the treatment of Parkinson's disease
AUTHOR(S): Wiseman, Lynda R.; Fitton, Andrew
CORPORATE SOURCE: Adis International Limited, Auckland, N. Z.
SOURCE: CNS Drugs (1999), 12(6), 485-497
CODEN: CNDREF; ISSN: 1172-7047
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 59 refs. The dopamine agonist cabergoline has been most widely studied as an adjuvant to levodopa/carbidopa therapy in patients with advanced Parkinson's disease experiencing response fluctuations ("wearing-off" and "on-off" phenomena) to long term levodopa therapy. Significant improvements in Unified Parkinson's Disease Rating Scale (UPDRS) scores for motor function and activities of daily living were observed with cabergoline in a placebo-controlled study in

this patient group. In addition, cabergoline significantly reduced "off" time compared with placebo after 12 and 24 wk' therapy. The requirement for levodopa to control symptoms of Parkinson's disease is reduced in patients given adjuvant cabergoline; however, the duration of this effect remains unclear. To date, adjuvant cabergoline has been shown to control the symptoms of advanced Parkinson's disease for periods of up to 5 yr in noncomparative studies. Limited data indicate that cabergoline is at least as effective as bromocriptine in this patient group, but is more effective than pergolide in controlling certain disabilities associated with long term levodopa therapy (specifically nocturnal disabilities and motor function during the "off" period). In patients with early Parkinson's disease, de novo therapy with cabergoline was associated with a significantly lower risk of developing motor complications after 5 yr than de novo levodopa/carbidopa therapy in a single trial. The incidence of motor complications (≥ 1) in patients randomized to receive cabergoline (\pm levodopa/carbidopa as required) was 22.3 vs. 33.7% in patients given only levodopa/carbidopa ($p < 0.05$). After 5 yr, 64% of cabergoline recipients required addnl. levodopa/carbidopa; however, the dosage was significantly lower than that given to patients receiving only levodopa/carbidopa. UPDRS motor function scores were better in the levodopa/carbidopa group. The tolerability profile of cabergoline appears typical of a dopamine agonist. CNS disturbances (including visual hallucinations, confusion, dizziness/light-headedness, increased libido, increased dyskinesias, insomnia and somnolence) and gastric upset are the most common events, but are rarely severe. Clin. trials indicate that the tolerability of cabergoline is similar to that of bromocriptine, but may be better than pergolide. Conclusions: Cabergoline is useful for controlling symptoms in patients with advanced Parkinson's disease experiencing response fluctuations to long term levodopa therapy. Importantly, it appears to be valuable as de novo therapy in patients with early disease in terms of reducing the risk of motor complications. Its long elimination half-life (63 to 68 h) and long duration of action, which allow once daily administration, may prove advantageous in terms of attaining maximal symptom control.

OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS
RECORD (11 CITINGS)
REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 107 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 80

ACCESSION NUMBER: 1999093318 EMBASE
TITLE: Dopamine agonists.
AUTHOR: Factor, S.A. (correspondence)
CORPORATE SOURCE: Parkinson's Disease, Movement Disorder Center, Albany Medical Center, 215 Washington Avenue Extension, Albany, NY 12203, United States.
SOURCE: Medical Clinics of North America, (1999) Vol. 83, No. 2, pp. 415-443.
Refs: 94
ISSN: 0025-7125 CODEN: MCNAA9
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
006 Internal Medicine
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Apr 1999
Last Updated on STN: 1 Apr 1999

AB Dopamine agonists have been used in the treatment of Parkinson's disease (PD) since the mid 1970s. With the approval of two new agents in 1997, the number available in the United States is up to four; bromocriptine, pergolide, pramipexole, ropinirole. These agents differ in dopamine receptor affinities and chemical structure, which, in turn, may possibly result in differences in efficacy tolerability and safety. Dopamine have historically been used in combination with levodopa in patients with advanced PD, but indicators are now expanding. With is expansion comes increasing controversy. This article reviews dopamine receptor pharmacology and the results of the clinical trials that have used for agonists available in the United States as well as a discussion of three minor agonists.

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STN DUPLICATE 81

ACCESSION NUMBER: 1999:360951 BIOSIS
DOCUMENT NUMBER: PREV199900360951
TITLE: Constrictive pericarditis and pleuropulmonary disease linked to ergot dopamine agonist therapy (Cabergoline) for Parkinson's disease.
AUTHOR(S): Ling, Lieng H.; Ahlskog, J. Eric [Reprint author]; Munger, Thomas M.; Limper, Andrew H.; Oh, Jae K.
CORPORATE SOURCE: Department of Neurology, Mayo Clinic Rochester, 200 First Street SW, Rochester, MN, 55905, USA
SOURCE: Mayo Clinic Proceedings, (April, 1999) Vol. 74, No. 4, pp. 371-375. print.
CODEN: MACPAJ. ISSN: 0025-6196.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Sep 1999
Last Updated on STN: 2 Sep 1999

AB Cabergoline is one of several ergoline dopamine agonist medications used in the treatment of Parkinson's disease (PD). We diagnosed constrictive pericarditis (CP) in a patient with PD receiving cabergoline therapy (10 mg daily), who had symptoms and signs of congestive heart failure (CHF). In the absence of previous reported cases of this condition linked to ergoline drugs, cabergoline was not initially identified as the cause. Shortly thereafter, however, the patient developed of a severe pleuropulmonary inflammatory-fibrotic syndrome, a recognized complication of ergoline medications, thus suggesting a common pathogenesis due to cabergoline therapy. To our knowledge, this is the first case in the English literature, although we speculate that CP may be more common than reported among patients with PD who are treated with an ergoline drug (cabergoline, bromocriptine, pergolide, or lisuride). The diagnosis of CP is difficult and requires a high level of suspicion; symptoms may masquerade as CHF due to common mechanisms such as coronary artery disease. In patients with PD who are taking not only cabergoline but also one of the other ergoline drugs, CP should be suspected if symptoms of CHF develop.

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ACCESSION NUMBER: 2000014664 EMBASE
TITLE: [Cabergoline versus pergolide: A video-blinded, randomised multicenter cross-over study].
Cabergolin versus pergolid: Eine videoverblindete, randomisierte, multizentrische cross-over-studie.
AUTHOR: Ulm, Gudrun (correspondence)
CORPORATE SOURCE: Paracelsus-Elena Klinik, Klinikstr. 16, 34128 Kassel, Germany.
AUTHOR: Schuler, P.
CORPORATE SOURCE: Pharmacia and Upjohn, Erlangen, Germany.

SOURCE: Aktuelle Neurologie, (Dec 1999) Vol. 26, No. 8,
pp. 360-365.
Refs: 13
ISSN: 0302-4350 CODEN: AKNUAR

COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: German
SUMMARY LANGUAGE: English; German
ENTRY DATE: Entered STN: 20 Jan 2000
Last Updated on STN: 20 Jan 2000

AB Methods: The efficacy and tolerability of cabergoline was investigated in a crossover trial versus pergolide. The investigation was performed in 48 patients with progressed Parkinson syndrome, suffering from late motor complications after L-dopa therapy (wearing off, on/off-fluctuations and dyskinesias). Primary endpoint was the UPDRS III-score (motor performance) in a video-blinded assessment. For this blinded evaluation, patients were investigated according to the items of UPDRS III in a standardized mode and this investigation was documented on videotapes. The videocassettes were randomized and a single experienced evaluator scored the tapes in a blinded manner. Results: Cabergoline showed at least equal efficacy when given once daily up to 6 mg compared to pergolide, given t.i.d. up to 5 mg in total. The trend showed a superiority for the cabergoline group for improvement of Off-phases. The same is true for the unblinded evaluation of UPDRS I. The unblinded evaluation of UPDRS III reached statistical significance ($p < 0.05$). The tolerability of cabergoline was better than the one of pergolide with less withdrawals, less serious adverse events and less adverse events. The duration and severity of the dyskinesias measured by UPDRS IV was lower with cabergoline. This finding was supported by the evaluation of the patient's diaries. In these diaries, the On-periods with obvious or very obvious dyskinesias were reduced up to 50 % compared to pergolide. Conclusion: The theoretic advantage of a continuous receptor-stimulation with thus reduced dyskinesias could be supported by this clinical trial. Consequently, after having finished the second treatment period, 63 % of all patients preferred a long-term treatment with cabergoline.

L9 ANSWER 110 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 83

ACCESSION NUMBER: 1999:112911 CAPLUS
DOCUMENT NUMBER: 130:306470
TITLE: Functional potencies of new antiparkinsonian drugs at recombinant human dopamine D1, D2 and D3 receptors
AUTHOR(S): Perachon, Sylvie; Schwartz, Jean-Charles; Sokoloff, Pierre
CORPORATE SOURCE: Unite de Neurobiologie et Pharmacologie Moleculaire, Centre Paul Broca de l'INSERM, Paris, F-75014, Fr.
SOURCE: European Journal of Pharmacology (1999), 366(2/3), 293-300
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We measured the affinities of bromocriptine, pramipexole, pergolide and ropinirole at human recombinant dopamine D1, D2 and D3 receptors in binding and functional tests. All four compds. bound with high affinity at the dopamine D3 receptor; bromocriptine and pergolide also had high affinity for the dopamine D2 receptor, while only pergolide had significant, although moderate, affinity for the dopamine D1 receptor. Only pergolide had high potency and intrinsic activity at the dopamine D1 receptor for stimulating

cAMP accumulation. In addition, the potencies and efficacies of pergolide and bromocriptine, as well as that of dopamine, at the dopamine D1 receptor were increased in the presence of forskolin, an adenylate cyclase activator. All four compds. were highly potent agonists at dopamine D2 and D3 receptors, as measured in a mitogenesis assay. Bromocriptine was ten times more potent and pramipexole and ropinirole ten times less potent at the dopamine D2 than at the dopamine D3 receptor, whereas pergolide was equipotent at the two receptors. These results suggest that the activity of recently developed antiparkinsonian drugs at either the dopamine D1 or the dopamine D3 and not only the dopamine D2 receptors should be taken into account in analyses of their mechanisms of action in therapeutics.

OS.CITING REF COUNT: 51 THERE ARE 51 CAPLUS RECORDS THAT CITE THIS RECORD (51 CITINGS)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 111 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 84

ACCESSION NUMBER: 1999:688738 CAPLUS

DOCUMENT NUMBER: 131:281493

TITLE: Modification of dopamine D2 receptor activity by pergolide in Parkinson's disease: an in vivo study by PET

AUTHOR(S): Linazasoro, Gurutz; Obeso, Jose A.; Gomez, Juan C.; Martinez, Mercedes; Antonini, Angelo; Leenders, Klaus L.

CORPORATE SOURCE: Center for Neurology and Functional Neurosurgery, Center for Neurology and Functional Neurosurgery, Clinica Quiron, San Sebastian, 20012, Spain

SOURCE: Clinical Neuropharmacology (1999), 22(5), 277-280

CODEN: CLNEDB; ISSN: 0362-5664

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB It is well known that chronic administration of pergolide and other dopamine agonists may induce a down-regulation of dopamine D2 receptors in the rat model of Parkinson's disease (PD). To our knowledge, this effect has not been demonstrated in vivo in patients with PD. At present, the status of striatal dopamine D2 receptors can be studied with use of positron emission tomog. (PET) technol. Five patients with PD chronically treated with levodopa were studied with use of PET and [11 C]-raclopride before and after 6 mo of pergolide treatment (dose range = 4.5-7.5 mg/d). We found a slight reduction in the specific striatal [11 C]-raclopride uptake index (mean reduction 14% in putamen and 9% in caudate) after pergolide treatment. This reduction appears to be related to down-regulation of the receptor, although competitive binding of pergolide at the D2 receptor cannot be excluded.

OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 112 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 85

ACCESSION NUMBER: 1999:150305 CAPLUS

DOCUMENT NUMBER: 130:261327

TITLE: Ropinirole: a dopamine agonist for the treatment of Parkinson's disease

AUTHOR(S): Kuzel, Mary D.

CORPORATE SOURCE: Pharmacy Practice, College of Pharmacy, North Dakota State University, Fargo, ND, 58103, USA

SOURCE: American Journal of Health-System Pharmacy (

1999), 56(3), 217-224

CODEN: AHSPEK; ISSN: 1079-2082

PUBLISHER: American Society of Health-System Pharmacists

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 42 refs. The pharmacol., pharmacokinetics, clin. efficacy, adverse effects, dosage and administration, and formulary considerations of ropinirole are reviewed. Ropinirole is a nonergoline dopamine agonist that binds to dopamine D2-receptors; the drug is indicated for use in the symptomatic treatment of early and late Parkinson's disease (PD). Ropinirole is rapidly absorbed after oral administration and undergoes extensive hepatic metabolism to active metabolites. The elimination half-life av. about six hours. Ropinirole has a low potential to interact with other drugs likely to be administered to PD patients. In patients with early PD, initial monotherapy with ropinirole was more effective than placebo or bromocriptine in the absence of selegiline and was as effective as bromocriptine in the presence of selegiline. Ropinirole was as effective as levodopa in patients with earlier stages of PD. In one subset of patients with advanced PD not adequately controlled by levodopa, adjunctive ropinirole was more effective than placebo and bromocriptine. Ropinirole was more effective than bromocriptine in patients previously given high-dose levodopa and was as effective in patients previously given low-dose levodopa or adjunctive dopamine agonist therapy. The most frequent adverse effects are nausea, somnolence, and dizziness; the dosage should be increased gradually to minimize adverse effects. Ropinirole is less expensive than bromocriptine and pergolide and similar in cost to pramipexole. Ropinirole appears to be a useful addition to existing therapeutic approaches to PD and is approved for both early and later stages of the disease.

OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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STN DUPLICATE 86

ACCESSION NUMBER: 1999:318902 BIOSIS

DOCUMENT NUMBER: PREV199900318902

TITLE: Differentiation of dopamine agonists and their role in the treatment of Parkinson's disease.

AUTHOR(S): Calne, D. B. [Reprint author]

CORPORATE SOURCE: Vancouver Hospital and Health Sciences Centre, 2221
Wesbrook Mall, Purdy Pavilion, Room M36, Vancouver, BC, V6T
2B5, Canada

SOURCE: Journal of Neural Transmission Supplement, (1999)
Vol. 56, No. 0, pp. 185-192. print.
CODEN: JNTSD4. ISSN: 0303-6995.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 17 Aug 1999

Last Updated on STN: 17 Aug 1999

AB Since the pioneering work of Hornykiewicz and his colleagues, it has been recognized that dopaminergic cells die selectively in Parkinson's disease, and considerable improvement in symptoms can be achieved by administering levodopa, so that it may be converted to dopamine. However, levodopa has side-effects, and its duration of action is relatively brief. For these reasons, alternative approaches have been undertaken to stimulate the dopamine receptors. In particular, artificial agonists for dopamine receptors have been developed. The pioneer compound was bromocriptine, which stimulates the D2 family of receptors. Bromocriptine is an ergot derivative, and other compounds that are structurally related to ergot have been developed. In particular, lisuride and

pergolide have been used for several years. Recently, an ergot derivative with an exceptionally long plasma half-life has been studied, cabergoline. Now there are also non-ergot derivatives that are D2 agonists, and are likely to have a role in the treatment of Parkinson's disease. Both ropinirole and pramipexole fall into this category, and each has been released in various countries for the treatment of Parkinson's disease. All of these compounds stimulate the D2 family of receptors, but they have varying actions on the D1 family of receptors. At present, there is no definite information on the role of the D1 family of receptors in either the therapeutic response to levodopa, or the development of adverse reactions. However, preliminary studies with a D1 agonist, ABT-431, are now in progress.

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ACCESSION NUMBER: 1999120482 ESBIODASE
TITLE: Differentiation of dopamine agonists and their role in
the treatment of Parkinson's disease
AUTHOR(S): Calne, Donald B.
CORPORATE SOURCE: Calne, Donald B. (Vancouver Hosp. and Hlth. Sci. Ctr.,
Vancouver, BC (CA)); Calne, Donald B. (F.R.C.P.C.
Vancouver Hosp. Hlth. S., Purdy Pavilion, 2221 Wesbrook
Mall, Vancouver, BC V6T 2B5 (CA))
SOURCE: Journal of Neural Transmission, Supplement
(1999), Number 56, pp. 185-192, 29 refs.
CODEN: JNTSD4 ISSN: 0303-6995
COUNTRY OF PUBLICATION: Austria
DOCUMENT TYPE: Journal; (Conference Paper)
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jan 2009
Last updated on STN: 31 Jan 2009

AN 1999120482 ESBIODASE

AB Since the pioneering work of Hornykiewicz and his colleagues, it has been recognized that dopaminergic cells die selectively in Parkinson's disease, and considerable improvement in symptoms can be achieved by administering levodopa, so that it may be converted to dopamine. However, levodopa has side-effects, and its duration of action is relatively brief. For these reasons, alternative approaches have been undertaken to stimulate the dopamine receptors. In particular, artificial agonists for dopamine receptors have been developed. The pioneer compound was bromocriptine, which stimulates the D2 family of receptors. Bromocriptine is an ergot derivative, and other compounds that are structurally related to ergot have been developed. In particular, lisuride and pergolide have been used for several years. Recently, an ergot derivative with an exceptionally long plasma half-life has been studied, cabergoline. Now there are also non-ergot derivatives that are D2 agonists, and are likely to have a role in the treatment of Parkinson's disease. Both ropinirole and pramipexole fall into this category, and each has been released in various countries for the treatment of Parkinson's disease. All of these compounds stimulate the D2 family of receptors, but they have varying actions on the D1 family of receptors. At present, there is no definite information on the role of the D1 family of receptors in either the therapeutic response to levodopa, or the development of adverse reactions. However, preliminary studies with a D1 agonist, ABT-431, are now in progress.

L9 ANSWER 115 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 87

ACCESSION NUMBER: 1999:223845 BIOSIS
DOCUMENT NUMBER: PREV199900223845

TITLE: Pergolide potentiates L-DOPA-induced dopamine release in
rat striatum after lesioning with 6-hydroxydopamine.
AUTHOR(S): Dethy, S. [Reprint author]; Laute, M. A.; Damhaut, P.;
Goldman, S.
CORPORATE SOURCE: Service de Neurologie, ULB-Hopital Erasme, 808, route de
Lennik, B-1070, Brussels, Belgium
SOURCE: Journal of Neural Transmission, (1999) Vol. 106,
No. 2, pp. 145-158. print.
CODEN: JNGSE8. ISSN: 0300-9564.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jun 1999
Last Updated on STN: 7 Jun 1999

AB We used intrastriatal microdialysis to study the effect of
pergolide, a D1/D2 dopamine (DA) receptor agonist on
biotransformation of exogenous L-DOPA in hemi-Parkinsonian rats.
DA and metabolites were assayed by microbore liquid chromatography.
Pergolide (50 µg/kg, i.p) caused a 67% and 87% decrease in
striatal EC levels of DA in intact and denervated striatum respectively.
In intact striatum but not in denervated striatum, pergolide
decreased EC levels of 3,4-dihydroxyphenylacetic acid (DOPAC) and
homovanillic acid (HVA) (53% and 42% decrease, respectively). L-DOPA (100
mg/kg, i.p.) produced significant increase in EC levels of DA, DOPAC and
HVA in intact and denervated striatum with and without local perfusion of
10⁻⁴ M pergolide. In denervated striatum, L-DOPA-induced DA
increase was significantly higher in rats with pergolide. Our
results suggest that, in an animal model of Parkinson's disease,
pergolide in association with L-DOPA favors the restoration of
striatal EC DA levels.

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ACCESSION NUMBER: 2000132351 EMBASE
TITLE: Iliocaval venous obstruction in pergolide-induced
retroperitoneal fibrosis.
AUTHOR: Simms, M.S. (correspondence)
CORPORATE SOURCE: Department of Urology, City Hospital, Hucknall Road,
Nottingham NG5 1PB, United Kingdom.
AUTHOR: Simms, M.H.
CORPORATE SOURCE: Department of Vascular Surgery, Selly Oak Hospital, Selly
Oak, Birmingham, United Kingdom.
SOURCE: Phlebology, (1999) Vol. 14, No. 3, pp. 126-127.
Refs: 4
ISSN: 0268-3555 CODEN: PHLEEF
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 27 Apr 2000
Last Updated on STN: 27 Apr 2000

AB Design: Case report. Setting: BMI Priory Hospital, Birmingham, UK.
Patient: A 67-year-old man presenting with unilateral lower limb oedema.
Past history included ipsilateral lower limb melanoma and
Parkinson's disease, treated by pergolide.
Intervention: Laparotomy to confirm a diagnosis of retroperitoneal
fibrosis (RPF) causing iliac vein obstruction. Conclusion: RPF is a rare

complication of pergolide therapy for Parkinson's disease. Previous reports have also described ilio caval obstruction and there may be an association between pergolide-induced RPF and venous complications.

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ACCESSION NUMBER: 1999280119 EMBASE
TITLE: Long term role of pergolide as an adjunct therapy in Parkinson's disease: Influence on disability, blood pressure, weight and levodopa syndrome.
AUTHOR: Sharma, J.C. (correspondence); Ross, I.N.
CORPORATE SOURCE: Newark Hospital, Newark, Nottinghamshire NG24 4DE, United Kingdom. jsharma@lineone.net
SOURCE: Parkinsonism and Related Disorders, (Sep 1999) Vol. 5, No. 3, pp. 111-114.
Refs: 15
ISSN: 1353-8020 CODEN: PRDIFO
PUBLISHER IDENT.: S 1353-8020(99)00017-6
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
006 Internal Medicine
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 26 Aug 1999
Last Updated on STN: 26 Aug 1999

AB Pergolide is a dopamine agonist acting on D1 and D2 receptors and has been used as an adjunct therapy with levodopa. We have retrospectively investigated its role over a duration of upto six years in Parkinson's disease (PD) patients to study: (1) its influence on the progression of disability related to PD; (2) effect on blood pressure and weight during the treatment period; (3) whether the use of pergolide has a long term levodopa sparing effect; (4) and how is it tolerated during this period? We studied 43 patients who had been on adjunct therapy with pergolide in addition to levodopa for more than six months. Mean age was 66 years, mean duration of PD prior to adding pergolide was 8 years and final assessment was done after a mean duration of adjunct therapy of 29 (6-72) months. There was no progression of disease disability as assessed on Hoehn and Yahr stage ($p = 0.09$) and Webster score ($p = 0.20$), while there was an improvement in symptom score ($p = 0.001$). There was an insignificant reduction in the dose of levodopa at final assessment from 630 to 535 mg ($p = 0.06$). A significant number of patients were able to discontinue taking selegiline ($p = 0.002$). There was no change in the number of patients with hallucinations ($p = 0.15$) and dyskinesia ($p = 0.09$). There was a significant fall in weight ($p = 0.02$), systolic ($p = 0.023$) and diastolic blood pressure ($p = 0.03$). This fall did not correlate with age, dose of pergolide or levodopa or disease severity but was influenced by duration of treatment. Ten patients discontinued pergolide for minor reasons after a mean duration of therapy for 23 months. We conclude that pergolide is a valuable adjunct therapy with levodopa over a duration of upto six years to maintain control of motor symptoms of Parkinson's disease.

L9 ANSWER 118 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 90

ACCESSION NUMBER: 1999:809431 CAPLUS
DOCUMENT NUMBER: 132:235383
TITLE: Hydroxyl radical and superoxide dismutase in blood of

patients with Parkinson's disease: relationship to clinical data

AUTHOR(S): Ihara, Yuetsu; Chuda, Masaki; Kuroda, Shigetoshi; Hayabara, Toshiyuki

CORPORATE SOURCE: Clinical Research Institute and Department of Neurology, National Minamiokayama Hospital, Okayama, 701-0304, Japan

SOURCE: Journal of the Neurological Sciences (1999), 170(2), 90-95
CODEN: JNSCAG; ISSN: 0022-510X

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hydroxyl radical (\cdot OH) levels in the blood and superoxide dismutase (SOD) activity in the plasma (plasma-SOD), SOD activity in red blood cells (RBC) relative to Cu,Zn-SOD (SOD1) protein (RBC-SOD/SOD1), SOD1 protein in RBC (SOD1/RBC) and plasma (SOD1/plasma), and Mn-SOD protein in plasma (SOD2/plasma) were measured in patients with Parkinson's disease (PD), multiple-system atrophy (MSA) with parkinsonism, and in control subjects. Patients with PD had higher \cdot OH and plasma-SOD values and lower RBC-SOD/SOD1 and SOD1/RBC values than the corresponding MSA and control values. In PD, RBC-SOD/SOD1 values were lower in older patients and were neg. correlated with age. \cdot OH levels were higher in PD patients with early onset, a long period of illness or severe Yahr stage, and were neg. correlated with onset and pos. correlated with duration of illness. RBC-SOD/SOD1 values in PD patients who received pergolide therapy were higher than those in PD patients who received neither pergolide nor bromocriptine therapy. Therefore, the higher \cdot OH level and the lower SOD1 activity may play a role in the onset and progression of PD, and pergolide may act neuroprotectively by inducing SOD1 activity.

OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 119 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 91

ACCESSION NUMBER: 1999079082 EMBASE

TITLE: Pericardial, retroperitoneal, and pleural fibrosis induced by pergolide.

AUTHOR: Shaunak, S., Dr. (correspondence); Wilkins, A.; Pilling, J.B.; Dick, D.J.

CORPORATE SOURCE: Department of Neurology, Norfolk and Norwich Hospital, Brunswick Road, Norwich NR1 3SR, United Kingdom.

AUTHOR: Shaunak, S., Dr. (correspondence)

CORPORATE SOURCE: Department of Neurology, Addenbrookes Hospital, Hills Road, Cambridge CB2 2QQ, United Kingdom.

SOURCE: Journal of Neurology Neurosurgery and Psychiatry, (Jan 1999) Vol. 66, No. 1, pp. 79-81.
Refs: 10
ISSN: 0022-3050 CODEN: JNNPAU

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 11 Mar 1999
Last Updated on STN: 11 Mar 1999

AB Three patients with Parkinson's disease are described who

developed pericardial, retroperitoneal, and pleural fibrosis associated with pergolide treatment. Surgical intervention was required in all three cases, either to reach a tissue diagnosis or for potentially life threatening complications. Symptoms emerged on average 2 years after the institution of treatment, and were sufficiently non-specific to cause significant delays in diagnosis in all cases. The erythrocyte sedimentation rate (ESR) was raised in the two patients in whom it was measured. Serosal fibrosis is a rarely reported adverse effect of pergolide treatment, although it is well described with other dopamine agonists. We suggest that patients with Parkinson's disease who receive pergolide treatment should be regularly monitored for the development of such complications.

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ACCESSION NUMBER: 1999050371 EMBASE
 TITLE: [Severe treatment-resistant depression proceeding Parkinson's disease].
 Schwere therapieresistente depression als erstmanifestation eines morbus Parkinson.
 AUTHOR: Amann, Benedikt, Dr. (correspondence)
 CORPORATE SOURCE: Psychiat. Klin. der Universitat, Nussbaumstrasse 7, D-80336 Munchen, Germany.
 AUTHOR: Erfurth, Andreas; Back, Tobias; Grunze, Heinz
 AUTHOR: Amann, Benedikt, Dr. (correspondence)
 CORPORATE SOURCE: Psychiatrische Klin. der Universitat, Nussbaumstrasse 7, D-80336 Munchen, Germany.
 SOURCE: Psychiatrische Praxis, (Jan 1999) Vol. 26, No. 1, pp. 45-47.
 Refs: 13
 ISSN: 0303-4259 CODEN: PSPXAT
 COUNTRY: Germany
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 032 Psychiatry
 037 Drug Literature Index
 008 Neurology and Neurosurgery
 LANGUAGE: German
 SUMMARY LANGUAGE: English; German
 ENTRY DATE: Entered STN: 4 Mar 1999
 Last Updated on STN: 4 Mar 1999

AB A 60-year old female patient was referred to our University hospital with the diagnosis of severe treatment-resistant major depression to perform electroconvulsive therapy (ECT). For almost two years the patient had been treated with several antidepressants and, temporarily, neuroleptics. After showing no favourable response to ECT, the diagnosis of idiopathic Parkinson's disease was made and the patient was treated with L-dopa plus benserazide and pergolide in combination with the monoamine oxidase inhibitor moclobemide. Both depressed mood and motor symptoms showed dramatic improvement under this therapy.

L9 ANSWER 121 OF 331 MEDLINE on STN DUPLICATE 93

ACCESSION NUMBER: 1999381064 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10451757
 TITLE: Ropinirole and pramipexole, the new agonists.
 AUTHOR: Hobson D E; Pourcher E; Martin W R
 CORPORATE SOURCE: University of Manitoba, Winnipeg, Canada.
 SOURCE: The Canadian journal of neurological sciences. Le journal canadien des sciences neurologiques, (1999 Aug) Vol. 26 Suppl 2, pp. S27-33. Ref: 53
 Journal code: 0415227. ISSN: 0317-1671.
 PUB. COUNTRY: Canada
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 12 Oct 1999
Last Updated on STN: 12 Oct 1999
Entered Medline: 28 Sep 1999

AB Ropinirole and pramipexole are non-ergoline dopamine agonists which are relatively specific for the D2 family of dopamine receptors. They have side-effect profiles linked to peripheral and central dopaminergic stimulation, amenable to tolerance through a slow titration or the addition of domperidone in sensitive patients. They do not have the uncommon but problematic ergot-related side effects of bromocriptine and pergolide. Ropinirole and pramipexole have both been shown to be efficacious when used as monotherapy in early Parkinson's disease (PD), and have been suggested as being less likely than levodopa to lead to the early development of motor fluctuations and dyskinesias in this clinical setting. They have also been shown to be useful as adjunctive therapy to levodopa in advanced PD and to have a levodopa-sparing effect in these patients. Dose equivalents amongst the available dopamine agonists is difficult to know with certainty but has been estimated as follows: 30 mg of bromocriptine, 15 mg of ropinirole, 4.5 mg of pramipexole, and 3.0 mg of pergolide.

L9 ANSWER 122 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 94

ACCESSION NUMBER: 2000:74499 CAPLUS
DOCUMENT NUMBER: 133:588
TITLE: The pivotal role of iron in NF- κ B activation and nigrostriatal dopaminergic neurodegeneration: Prospects for neuroprotection in Parkinson's disease with iron chelators
AUTHOR(S): Youdim, M. B. H.; Grunblatt, E.; Mandel, S.
CORPORATE SOURCE: Technion, Faculty of Medicine, Eve Topf and US National Parkinson's Foundation Centers for, Haifa, Israel
SOURCE: Annals of the New York Academy of Sciences (1999), 890(Neuroprotective Agents), 7-25
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB R-Apomorphine (APO) the catechol-derived dopamine D1-D2 receptor agonist has been shown to be highly potent iron chelator and radical scavenger and inhibitor of membrane lipid peroxidn. in vitro, in vivo and in cell culture employing PC12 cells. Its potency has been compared to the prototype iron chelator desferrioxamine (desferal), dopamine, nifedipine and dopamine D2 receptor agonists, bromocriptine, lisuride, pergolide and pramipexole. APO also inhibits brain and mitochondrial protein oxidation In vivo APO protects against MPTP (N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine)-induced striatal dopaminergic neurodegeneration in C57 black mice with as low as 5 mg/kg. APO is a reversible competitive inhibitor of monoamine oxidase (MAO) A and B with IC50 values of 93 and 214 uM, resp. The iron chelating and radical scavenging actions of desferal and APO explains their ability to inhibit iron and 6-hydroxydopamine (6-OHDA)-induced neurodegeneration and activation of redox-sensitive transcription factor NF- κ B and the subsequent transactivation of promoters of genes involved in inflammatory cytokines. Iron is thought to play a pivotal role in neurodegeneration, and APO may be an ideal drug to investigate neuroprotection in Parkinson's disease where iron and oxidative stress have been implicated in the pathogenesis of nigrostriatal dopamine neuron degeneration.

OS.CITING REF COUNT: 56 THERE ARE 56 CAPLUS RECORDS THAT CITE THIS
RECORD (56 CITINGS)
REFERENCE COUNT: 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ACCESSION NUMBER: 1999281621 EMBASE
TITLE: Ropinirole and pramipexole, the new agonists.
AUTHOR: Hobson, Douglas E.
CORPORATE SOURCE: University of Manitoba, Winnipeg, Man., Canada.
AUTHOR: Pourcher, Emmanuelle
CORPORATE SOURCE: Laval University, Quebec City, Que., Canada.
AUTHOR: Martin, W.R. Wayne (correspondence)
CORPORATE SOURCE: University of Alberta, Edmonton, Alta., Canada.
AUTHOR: Martin, W.R. Wayne (correspondence)
CORPORATE SOURCE: Movement Disorder Clinic, Glenrose Rehabilitation Hospital,
10230-III Avenue, Edmonton, Alta. T5G 0B7, Canada.
SOURCE: Canadian Journal of Neurological Sciences, (1999)
Vol. 26, No. SUPPL. 2, pp. S27-S33.
Refs: 53
ISSN: 0317-1671 CODEN: CJNSA2
COUNTRY: Canada
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 26 Aug 1999
Last Updated on STN: 26 Aug 1999

AB Ropinirole and pramipexole are non-ergoline dopamine agonists which are relatively specific for the D2 family of dopamine receptors. They have side- effect profiles linked to peripheral and central dopaminergic stimulation, amenable to tolerance through a slow titration or the addition of domperidone in sensitive patients. They do not have the uncommon but problematic ergot- related side effects of bromocriptine and pergolide. Ropinirole and pramipexole have both been shown to be efficacious when used as monotherapy in early Parkinson's disease (PD), and have been suggested as being less likely than levodopa to lead to the early development of motor fluctuations and dyskinesias in this clinical setting. They have also been shown to be useful as adjunctive therapy to levodopa in advanced PD and to have a levodopa-sparing effect in these patients. Dose equivalents amongst the available dopamine agonists is difficult to know with certainty but has been estimated as follows: 30 mg of bromocriptine, 15 mg of ropinirole, 4.5 mg of pramipexole, and 3.0 mg of pergolide.

L9 ANSWER 124 OF 331 Elsevier Biobase COPYRIGHT 2009 Elsevier Science B.V.
on STN

ACCESSION NUMBER: 1999185044 ESBIODBASE
TITLE: Ropinirole and pramipexole, the new agonists
AUTHOR(S): Hobson, Douglas E.; Pourcher, Emmanuelle; Martin, W.R.
Wayne
CORPORATE SOURCE: Hobson, Douglas E. (University of Manitoba, Winnipeg,
Man. (CA)); Pourcher, Emmanuelle (Laval University,
Quebec City, Que. (CA)); Martin, W.R. Wayne (University
of Alberta, Edmonton, Alta. (CA)); Martin, W.R. Wayne
(Movement Disorder Clinic, Glenrose Rehabilitation
Hospital, 19, 10230-111 Avenue, Edmonton, Alta. T5G 0B7

(CA))
SOURCE: Canadian Journal of Neurological Sciences
(1999) Volume 26, Number SUPPL. 2, 53 refs.
CODEN: CJNSA2 ISSN: 0317-1671

COUNTRY OF PUBLICATION: Canada
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 31 Jan 2009
Last updated on STN: 31 Jan 2009

AN 1999185044 ESBIODASE

AB Ropinirole and pramipexole are non-ergoline dopamine agonists which are relatively specific for the D2 family of dopamine receptors. They have side-effect profiles linked to peripheral and central dopaminergic stimulation, amenable to tolerance through a slow titration or the addition of domperidone in sensitive patients. They do not have the uncommon but problematic ergot-related side effects of bromocriptine and pergolide. Ropinirole and pramipexole have both been shown to be efficacious when used as monotherapy in early Parkinson's disease (PD), and have been suggested as being less likely than levodopa to lead to the early development of motor fluctuations and dyskinesias in this clinical setting. They have also been shown to be useful as adjunctive therapy to levodopa in advanced PD and to have a levodopa-sparing effect in these patients. Dose equivalents amongst the available dopamine agonists is difficult to know with certainty but has been estimated as follows: 30 mg of bromocriptine, 15 mg of ropinirole, 4.5 mg of pramipexole, and 3.0 mg of pergolide.

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ACCESSION NUMBER: 1998177021 EMBASE

TITLE: [New treatment of Parkinson disease].
Nouveaux traitements de la maladie de Parkinson.

AUTHOR: Vingerhoets, F., Dr. (correspondence); Ghika, J.; Albanese, A.

CORPORATE SOURCE: Service de Neurologie, CHUV, 1011 Lausanne, France.

SOURCE: Medecine et Hygiene, (13 May 1998) Vol. 56, No. 2209, pp. 1028-1035.
Refs: 27

ISSN: 0025-6749 CODEN: MEHGAB

COUNTRY: Switzerland

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery

LANGUAGE: French

SUMMARY LANGUAGE: English; French

ENTRY DATE: Entered STN: 18 Jun 1998

Last Updated on STN: 18 Jun 1998

AB A wealth of new molecules appeared recently for the treatment of Parkinson's disease. New galenic presentations of L-dopa (biphasic Madopar DR) and COMT inhibitors (tolcapone, entacapone) prolong the effects of L-dopa. New potent, well-tolerated dopaminergic agonists (pergolide, ropinirole, pramipexole, and cabergoline) broaden the possibilities treating early and late phases of the disease and may provide some neuroprotection. Finally subthalamic and pallidal stimulations offer major improvements for advanced patients with drug-resistant fluctuations, but, with uncertainty on long term effects. These procedures should stay in the hands of an experienced team of neurologists and neurosurgeons. Neurotransplantation and use of growth factors are still in preclinical phases.

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DUPLICATE 95

ACCESSION NUMBER: 1998359120 EMBASE
TITLE: Efficiency and safety of bilateral contemporaneous pallidal stimulation (deep brain stimulation) in levodopa-responsive patients with parkinson's disease with severe motor fluctuations: A 2-year follow-up review.
AUTHOR: Ghika, Joseph, Dr. (correspondence); Villemure, Jean-Guy; Fankhauser, Heinz; Favre, Jacques; Assal, Gil; Ghika-Schmid, Florence
CORPORATE SOURCE: Serv. Neurol., Neurochirurg., N., Ctr. Hosp. Universitaire Vaudois, Lausanne, Switzerland. joseph.ghika@hospvd.ch
AUTHOR: Ghika, Joseph, Dr. (correspondence)
CORPORATE SOURCE: Service de Neurologie, Ctr. Hosp. Universitaire Vaudois, BH 13, CH-1011 Lausanne, Switzerland. joseph.ghika@hospvd.ch
SOURCE: Journal of Neurosurgery, (Nov 1998) Vol. 89, No. 5, pp. 713-718.
Refs: 58
ISSN: 0022-3085 CODEN: JONSAC
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Nov 1998
Last Updated on STN: 19 Nov 1998

AB Object. The aim of this study was to evaluate the long-term safety and efficacy of bilateral contemporaneous deep brain stimulation (DBS) in patients who have levodopa-responsive parkinsonism with untreatable motor fluctuations. Bilateral pallidotomy carries a high risk of corticobulbar and cognitive dysfunction. Deep brain stimulation offers new alternatives with major advantages such as reversibility of effects, minimal permanent lesions, and adapt-ability to individual needs, changes in medication, side effects, and evolution of the disease. Methods. Patients in whom levodopa-responsive parkinsonism with untreatable severe motor fluctuations has been clinically diagnosed underwent bilateral pallidal magnetic resonance image-guided electrode implantation while receiving a local anesthetic. Pre- and postoperative evaluations at 3-month intervals included Unified Parkinson's Disease Rating Scale (UPDRS) scoring, Hoehn and Yahr staging, 24-hour self- assessments, and neuropsychological examinations. Six patients with a mean age of 55 years (mean 42-67 years), a mean duration of disease of 15.5 years (range 12-21 years), a mean 'on/off' Hoehn and Yahr stage score of 3/4.2 (range 3-5), and a mean 'off' time of 40% (range 20-50%) underwent bilateral contemporaneous pallidal DBS, with a minimum follow-up period lasting 24 months (range 24-30 months). The mean dose of levodopa in these patients could not be changed significantly after the procedure and pergolide was added after 12 months in five patients because of recurring fluctuations despite adjustments in stimulation parameters. All but two patients had no fluctuations until 9 months. Two of the patients reported barely perceptible fluctuations at 12 months and two at 15 months; however, two patients remain without fluctuations at 2 years. The mean improvements in the UPDRS motor score in the off time and the activities of daily living (ADL) score were more than 50%; the mean off time decreased from 40 to 10%, and the mean dyskinesia and complication of treatment scores were reduced to one-third until pergolide was introduced at 12 months. No significant improvement in 'on' scores was observed. A slight worsening after 1 year was observed and three patients developed levodopa- and stimulation-resistant gait ignition failure and minimal fluctuations at 1 year. Side effects, which were controlled by modulation of stimulation, included dysarthria, dystonia, and confusion. Conclusions. Bilateral pallidal DBS is safe and efficient in patients who

have levodopa-responsive parkinsonism with severe fluctuations.
Major improvements in motor score, ADL score, and off time persisted
beyond 2 years after the operation, but signs of decreased efficacy
started to be seen after 12 months.

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ACCESSION NUMBER: 1998242199 EMBASE
TITLE: Apomorphine enantiomers protect cultured pheochromocytoma
(PC12) cells from oxidative stress induced by H₂O₂ and
6-hydroxydopamine.
AUTHOR: Gross, Aviva; Youdim, Moussa B.H., Dr. (correspondence)
CORPORATE SOURCE: Department of Pharmacology, Bruce Rappaport Family Research
Institute, Technion, Haifa, Israel.
AUTHOR: Gassen, Michael
CORPORATE SOURCE: Merck KGaA, Biomedical Research CNS, Darmstadt, Germany.
AUTHOR: Youdim, Moussa B.H., Dr. (correspondence)
CORPORATE SOURCE: Department of Pharmacology, Faculty of Medicine, Technion,
PO Box 9649, Haifa 31096, Israel.
SOURCE: Movement Disorders, (1998) Vol. 13, No. 4, pp.
661-667.
Refs: 23
ISSN: 0885-3185 CODEN: MOVDEA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 052 Toxicology
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 1998
Last Updated on STN: 6 Aug 1998

AB A significant body of evidence has been provided to support the hypothesis
that oxidant stress may be responsible for the degeneration of
dopaminergic neurons in the substantia nigra pars compacta in
Parkinson's disease. Apomorphine, a dopamine D(1)/D(2)-receptor
agonist in the clinical therapy of Parkinson's disease, has been
found to be a potent antioxidant and to prevent free radical reaction in
rat brain mitochondrial fraction. In this article we show that 1-10 μ M
of apomorphine protects rat pheochromocytoma (PC12) cells from the toxic
effects of H₂O₂ (0.6 mM) and the neurotoxin 6-hydroxydopamine (150
 μ M). Neither of these effects were exhibited by ascorbic acid,
desferal, lisuride, or bromocriptine. Although pergolide
exhibited some protection of PC12 cells against H₂O₂ toxicity, it was
not as potent as apomorphine. In light of the present findings and the
clinical reports that parkinsonian patients on long-term
apomorphine therapy stabilize clinically and can be weaned off L-dopa, one
may assume that apomorphine can exert a neuroprotective activity by way of
its potent antioxidant properties.

L9 ANSWER 128 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 97

ACCESSION NUMBER: 1998:784811 CAPLUS
DOCUMENT NUMBER: 130:148095
TITLE: Clinical pharmacology of dopamine agonists in
Parkinson's disease
AUTHOR(S): Lange, Klaus W.
CORPORATE SOURCE: Department of Neuropsychology and Behavioural
Neurobiology, University of Regensburg, Regensburg,
Germany
SOURCE: Drugs & Aging (1998), 13(5), 381-389
CODEN: DRAGE6; ISSN: 1170-229X
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 83 refs. Oral levodopa is the most effective symptomatic treatment for Parkinson's disease. Dopamine agonists are useful adjuvants to levodopa in the pharmacotherapy of parkinsonian patients. Monotherapy with dopamine agonists in early Parkinson's disease has been advocated in order to delay the occurrence of complications associated with long term administration of levodopa. The use of dopamine agonists alone provides an adequate antiparkinsonian effect in only a minority of patients. In early stages of Parkinson's disease, dopamine agonists can produce a clin. response comparable with levodopa but, thereafter, their efficacy wanes. Early initiation of combination therapy with levodopa and dopamine agonists appears to reduce the severity and delay the appearance of the complications associated with long term administration of levodopa. Currently, dopamine agonists are most commonly used in combination with levodopa in patients in advanced stages of the disease who experience fluctuations of their motor symptoms. Despite their different pharmacodynamic and pharmacokinetic profiles, the ergot derivs. bromocriptine, lisuride and pergolide appear to be very similar in terms of their clin. efficacy. Continuous dopaminergic stimulation by parenteral infusion of water-soluble dopamine agonists such as apomorphine and lisuride can overcome motor fluctuations in advanced Parkinson's disease. Other dopamine agonists such as cabergoline, pramipexole and ropinirole are currently being studied. Further studies with these compds. will be required to determine their efficacy and adverse effects in comparison with the currently available orally active ergot agonists. It has been suggested that oxidative stress resulting from dopamine metabolism may be reduced by the administration of dopamine agonists. These drugs may therefore slow the rate of progression of Parkinson's disease. At present, however, there is no convincing clin. data to support a neuroprotective effect of dopamine agonists.

OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)

REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 129 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 98

ACCESSION NUMBER: 1999:5742 CAPLUS

DOCUMENT NUMBER: 130:205017

TITLE: A six-month study of pergolide and levodopa in de novo parkinson's disease patients

AUTHOR(S): Kulisevsky, Jaime; Lopez-Villegas, Dolores; Garcia-Sanchez, Carmen; Barbanoj, Manel; Gironell, Alexandre; Pascual-Sedano, Berta

CORPORATE SOURCE: Movement Disorders Section, Department of Neurology, Sant Pau Hospital, Autonomous University of Barcelona, Barcelona, 08025, Spain

SOURCE: Clinical Neuropharmacology (1998), 21(6), 358-362

CODEN: CLNEDB; ISSN: 0362-5664

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Formal studies examining the antiparkinsonian efficacy of levodopa and pergolide monotherapy in de novo Parkinson's disease (PD) are lacking. The authors conducted a preliminary, 6-mo, open-label parallel exptl. study with de novo consecutive PD patients who were randomly assigned to three daily doses of pergolide (n = 10; mean age, 63.7 yr; mean Hohen & Yahr score, 1.5; mean final dose, 2.8 mg daily) or levodopa (n = 10; mean age, 67.3 yr; mean Hohen & Yahr score, 1.8; mean final dose, 435 mg daily). Doses were titrated individually according to patients' evaluation of their own functional ability, known

side-effects, and a monthly administration of the Unified Parkinson's Disease Rating Scale (UPDRS) by a clinician blind to the treatment regime. All patients completed the study. There were no significant basal differences between groups and no significant treatment or treatment-by-time effects in UP-DRS scores (according to two-way ANOVA). A clear time effect was observed for most of the functional and motor variables ($p < 0.001$), with significant improvement during the first month that was maintained for the duration of the study in both groups. Side effects were mild, transient, and comparable. In this preliminary study, pergolide and levodopa exhibited similar symptomatic efficacy and incidence of side effects in the short-term treatment of de novo PD patients at their usual age of clin. manifestation.

OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS RECORD (11 CITINGS)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 130 OF 331 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation
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ACCESSION NUMBER: 1999:87547 SCISEARCH
THE GENUINE ARTICLE: 162HP
TITLE: Pergolide
AUTHOR: Lledo A (Reprint)
CORPORATE SOURCE: Eli Lilly Int Corp, Lilly Res Ctr, 13 Hanover Sq, London W1R OPA, England (Reprint)
AUTHOR: Lledo A (Reprint)
CORPORATE SOURCE: Eli Lilly Int Corp, Lilly Res Ctr, London W1R OPA, England
COUNTRY OF AUTHOR: England
SOURCE: AKTUELLE NEUROLOGIE, (DEC 1998) Vol. 25, Supp. [4], pp. S293-S294.
ISSN: 0302-4350.
PUBLISHER: GEORG THIEME VERLAG KG, RUDIGERSTR 14, D-70469 STUTTGART, GERMANY.
DOCUMENT TYPE: Article; Journal
LANGUAGE: German
REFERENCE COUNT: 12
ENTRY DATE: Entered STN: 1999
Last Updated on STN: 1999

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Pergolide is a dopamine agonist with affinity for D1, D2 and D3 receptors. Pergolide has a long half-life, is absorbed rapidly from the gastrointestinal tract, metabolised by the liver and excreted through the kidneys (55%), the faeces (40%) and the lungs (5%). Pergolide has proven to be an efficacious drug in treating Parkinson's disease in several studies. In a large study including 376 patients of pergolide given as concomitant medication to levodopa, a significant increase in motor scores as well as in on-time were reported. Moreover, this motor improvement correlated with an improvement in the activities of daily living. At the same time the levodopa dose could be decreased. In comparative studies against bromocriptine, pergolide has shown to be superior in most cases. Finally, in a recently presented study, pergolide used as a monotherapeutic drug in Parkinson's disease significantly improved UPDRS Part I "motoricity" and Part II "activities of daily living".

L9 ANSWER 131 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 99

ACCESSION NUMBER: 1998092198 EMBASE
TITLE: Apomorphine enantiomers protect cultured pheochromocytoma (PC12) cells from oxidative stress induced by H(2)O(2) and 6-hydroxydopamine.

AUTHOR: Youdim, Moussa B. H.
CORPORATE SOURCE: Department of Pharmacology, Faculty of Medicine, Technion,
PO Box 9649, Haifa 31096, Israel.
AUTHOR: Gassen, Michael; Gross, Aviva
AUTHOR: Youdin, M.B.H. (correspondence)
CORPORATE SOURCE: Department of Pharmacology, Faculty of Medicine, Technion,
PO Box 9649, Haifa 31096, Israel.
SOURCE: Movement Disorders, (1998) Vol. 13, No. 2, pp.
242-248.
Refs: 27
ISSN: 0885-3185 CODEN: MOVDEA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 Apr 1998
Last Updated on STN: 9 Apr 1998

AB A significant body of evidence has been provided to support the hypothesis that oxidant stress may be responsible for the degeneration of dopaminergic neurons in the substantia nigra pars compacta in Parkinson's disease. Apomorphine, a dopamine D(1)/D(2)-receptor agonist in the clinical therapy of Parkinson's disease, has been found to be a potent antioxidant and to prevent free radical reaction in rat brain mitochondrial fraction. In this article we show that 1-10 μ M of apomorphine protects rat pheochromocytoma (PC12) cells from the toxic effects of H(2)O(2) (0.6 mM) and the neurotoxin 6-hydroxydopamine (150 μ M). These effects were not exhibited by ascorbic acid, desferal, lisuride, or bromocriptine. Although pergolide exhibited some protection of PC12 cells against H(2)O(2) toxicity, it was not as potent as apomorphine. In light of the present findings and the clinical reports that parkinsonian patients on long-term apomorphine stabilize clinically and can be weaned off L-dopa, one may assume that apomorphine can exert a neuroprotective activity via its potent antioxidant properties.

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ACCESSION NUMBER: 1998:368728 BIOSIS
DOCUMENT NUMBER: PREV199800368728
TITLE: Therapeutic effects of dopamine D1/D2 receptor agonists on
detrusor hyperreflexia in
1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-lesioned
Parkinsonian cynomolgus monkeys.
AUTHOR(S): Yoshimura, Naoki; Mizuta, Eiji; Yoshida, Osamu; Kuno,
Sadako [Reprint author]
CORPORATE SOURCE: Dep. Neurol., Cent. Neurol. Dis., Utano Natl. Hosp.,
Narutaki, Kyoto 616-8255, Japan
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (
July, 1998) Vol. 286, No. 1, pp. 228-233. print.
CODEN: JPETAB. ISSN: 0022-3565.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Aug 1998
Last Updated on STN: 21 Oct 1998

AB The effects of dopamine receptor agonists on urinary bladder function were evaluated in normal and 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-lesioned parkinsonian cynomolgus monkeys to investigate the therapeutic efficacy in the treatment of urinary symptoms in Parkinson's disease. Under ketamine anesthesia, cystometrograms

exhibited significant reduction in the volume threshold for the micturition reflex in MPTP-lesioned parkinsonian monkeys when compared with those of normal monkeys. The selective dopamine D2 receptor agonist bromocriptine significantly reduced the bladder volume threshold for the micturition reflex by 25 to 30% in both normal and MPTP-lesioned animals. The nonselective D1/D2 receptor agonist pergolide significantly reduced the bladder volume threshold by 22% in normal monkeys, but increased the volume threshold by 50% in MPTP-lesioned parkinsonian monkeys. Another D1/D2 agonist (5R,8R,10R)-6-methyl-8-(1,2,4-triazol-1-ylmethyl) ergoline maleate (BAM-1110) also increased the bladder volume threshold (by 80%) in parkinsonian monkeys without significant effects on the micturition reflex in normal monkeys. The reduction in the volume threshold by bromocriptine in both normal and MPTP-treated groups and by pergolide in normal monkeys was suppressed by pretreatment with the selective D2 antagonist sulpiride, whereas the increment in the volume threshold by pergolide and BAM-1110 in parkinsonian monkeys was antagonized by pretreatment with the selective D1 antagonist SCH 23390, but not by sulpiride. These findings suggest that concurrent activation of D1/D2 receptors, rather than selective stimulation of D2 receptors, might be beneficial for treating urinary symptoms caused by detrusor hyperreflexia in Parkinson's disease.

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STN DUPLICATE 101

ACCESSION NUMBER: 1998:306594 BIOSIS
DOCUMENT NUMBER: PREV199800306594
TITLE: Pergolide scavenges both hydroxyl and nitric oxide free radicals in vitro and inhibits lipid peroxidative in different regions of the rat brain.
AUTHOR(S): Gomez-Vargas, Marvin [Reprint author]; Nishibayashi-Asanuma, Sakiko; Asanuma, Masato; Kondo, Yoichi; Iwata, Emi; Ogawa, Norio
CORPORATE SOURCE: Dep. Neurosci., Inst. Mol. Cell. Med., Okayama Univ. Med. Sch., 2-5-1 Shikatacho, Okayama 700-8558, Japan
SOURCE: Brain Research, (April 20, 1998) Vol. 790, No. 1-2, pp. 202-208. print.
CODEN: BRREAP. ISSN: 0006-8993.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Jul 1998
Last Updated on STN: 15 Jul 1998

AB The free radical hypothesis for the pathogenesis and/or progression of Parkinson's disease (PD) has gained wide acceptance in recent years. Although it is clear that dopamine (DA) agonists cannot completely replace levodopa therapy, they can be beneficial early in the course of PD by reducing the accumulation of DA which undergoes auto-oxidation and generates cytotoxic free radicals. In the present study we demonstrate that pergolide, a widely used DA agonist, has free radical scavenging and antioxidant activities. Using a direct detection system for nitric oxide radical (NOcntdot) by electron spin resonance (ESR) spectrometry in an in vitro cntdotNO-generating system, we examined the quenching effects of pergolide on the amount of NOcntdot generated. Pergolide dose-dependently scavenged NOcntdot. In the competition assay, the IC50 value for pergolide was estimated to be about 30 muM. Pergolide also dose-dependently attenuated the hydroxyl radical (cntdotOH) signal in an in vitro FeSO4-H2O2 ESR system with an approximate IC50 value of 300 muM. Furthermore, this agent significantly inhibited phospholipid peroxidation of rat brain homogenates in in vitro experiments and after repeated administration (0.5 mg/kg/24 h, i.p. for 7 days). Our findings suggest a neuroprotective role for pergolide on dopaminergic neurons due

to its free radical scavenging and antioxidant properties.

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ACCESSION NUMBER: 1998280302 EMBASE
TITLE: [New dopamine agonists for the treatment of Parkinson's disease].
Neue dopaminagonisten fur die therapie des morbus Parkinson.
AUTHOR: Pogarell, O., Dr. (correspondence); Oertel, W.H.
CORPORATE SOURCE: Neurologische Klinik, Philipps-Universitat Marburg.
AUTHOR: Pogarell, O., Dr. (correspondence)
CORPORATE SOURCE: Neurologische Klin. mit Poliklin., Philipps-Universitat Marburg, Rudolf-Bultmann-Strasse 8, 35033 Marburg, Germany.
AUTHOR: Pogarell, O., Dr. (correspondence)
CORPORATE SOURCE: Neurologische Klinik mit Poliklinik, Philipps-Universitat Marburg, Rudolf-Bultmann-Strasse 8, 35033 Marburg, Germany.
SOURCE: Aktuelle Neurologie, (Aug 1998) Vol. 25, No. 5, pp. 202-209.
Refs: 66
ISSN: 0302-4350 CODEN: AKNUAR
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: German
SUMMARY LANGUAGE: English; German
ENTRY DATE: Entered STN: 10 Sep 1998
Last Updated on STN: 10 Sep 1998

AB The development of motor fluctuations and dyskinesias remains a challenge in the treatment of advanced Parkinson's disease. These complications are associated with the dosage and duration of levodopa therapy, therefore a long-term levodopa monotherapy should be avoided. The early introduction of dopamine agonists and concomitant reduction of levodopa is considered to delay the occurrence of levodopa-associated complications and to improve already existing fluctuations. In addition to the established oral ergoline dopamine agonists bromocriptine, lisuride and pergolide new compounds have been developed and investigated in studies to further improve long-term therapy of Parkinson's disease. Dihydroergocriptine and cabergoline are also ergoline dopamine agonists. These drugs differ mainly with regard to pharmacokinetic properties (long plasma half-life) and affinity for dopamine D1 receptors. Ropinirole and pramipexole are two non-ergoline derivatives without affinity for D1 receptors but with high affinity for the dopamine D3 receptor subtype. Since comparative studies for most compounds are lacking, dopamine agonists should be selected according to individual efficacy and tolerability and cost effectiveness in the individual patient.

L9 ANSWER 135 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 103

ACCESSION NUMBER: 1998:681801 CAPLUS
DOCUMENT NUMBER: 130:61123
TITLE: Dopamine agonists in Parkinson's disease. What is their role in early treatment?
AUTHOR(S): Stocchi, Fabrizio
CORPORATE SOURCE: Department of Neuroscience, University "La Sapienza" of Rome and "Neuromed" Pozzilli (IS), Rome, Italy
SOURCE: CNS Drugs (1998), 10(3), 159-170
CODEN: CNDREF; ISSN: 1172-7047
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 68 refs. Dopamine receptor agonists are pharmacol. agents

with diverse phys. and chemical properties that share the capacity to stimulate dopamine receptors and provide an antiparkinsonian effect. Currently available dopamine agonists belong to 2 classes: ergot (bromocriptine, lisuride, pergolide, cabergoline) and non-ergot (apomorphine, ropinirole, pramipexole) derivs., each having a different pharmacol. profile and different affinity for the dopaminergic receptors and subtypes. Dopamine agonists act directly on striatal dopamine receptors. Unlike levodopa, they do not require metabolic conversion to an active form, and so their effects are independent of the degenerative state of dopaminergic terminals. They can selectively stimulate subclasses of dopamine receptors, theor. reducing the incidence of adverse effects. Dopamine agonists do not compete with circulating plasma amino acids for absorption and transport into the brain and they do not generate free radicals or induce oxidative stress. Recently it has been demonstrated that dopamine D2 receptor-selective agonists may protect against glutamate-induced neurotoxicity in cultured neurons. Dopamine agonists have been employed since 1974 as adjuncts to levodopa for patients with advanced Parkinson's disease. However, several studies have demonstrated the capacity of these drugs to improve motor fluctuations and reduce dyskinesia in parkinsonian patients whose response to levodopa is associated with motor complications. Moreover dopamine agonists provide a levodopa sparing effect. In the past some authors reported a clear symptomatic effect of dopamine agonists used in monotherapy in patients with de novo Parkinson's disease but because of the higher incidence of adverse effects compared with levodopa monotherapy this therapeutic strategy was not widely used. Recently the therapeutic approach to Parkinson's disease has begun to change and the role of dopamine agonists become more prominent especially in early treatment (i.e. in patients who have not previously received any other dopaminergic treatment for Parkinson's disease). There are now convincing animal studies which show that dopamine agonists induce less motor complications than levodopa when used as long term treatment. Clin. studies have shown that early treatment with dopamine agonists is associated with a lower incidence of motor fluctuations and dyskinesias. Controlled clin. trials have demonstrated that dopamine agonists may be as effective as levodopa in improving parkinsonian symptoms at least in the initial stages of the disease. Their use as initial therapy is therefore strongly recommended in young patients who have a higher risk of developing levodopa-induced motor complications. In elderly patients, cognitive impairment and cardiovascular disease are important modifiers in determining the appropriate pharmacol. intervention. The higher incidence of systemic adverse effects induced by dopamine agonists can be controlled with slow titration of dosage and co-administration of domperidone.

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ACCESSION NUMBER: 1998235349 EMBASE

TITLE: Prescribing pergolide in the elderly - An open label study of pergolide in elderly patients with Parkinson's disease.

AUTHOR: Hindle, J.V., Dr. (correspondence); Meara, R.J.; Sharma, J.C.; Medcalf, P.; Forsyth, D.R.; Huggett, I.M.; Cassidy, T.P.; Morris, J.; Dunn, A.; Hobson, J.P.

CORPORATE SOURCE: Consultant Physician Care of Elderly, Llandudno General Hospital, Llandudno, Conwy LL30 1LB, United Kingdom.

SOURCE: International Journal of Geriatric Psychopharmacology, (1998) Vol. 1, No. 2, pp. 78-81.

Refs: 13

ISSN: 1364-8233 CODEN: IJGPFT

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 020 Gerontology and Geriatrics
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 10 Sep 1998

Last Updated on STN: 10 Sep 1998

AB The aims of the study were to examine the prescription, clinical effectiveness and tolerability of the dopamine agonist pergolide in elderly patients with idiopathic Parkinson's disease. Pergolide was prescribed using individually tailored incremental doses or the manufacturer's start pack. An open label study including 74 patients (50 on tailored start and 24 on starter pack) was conducted. Pergolide was prescribed mainly for motor fluctuations but also allowed a small reduction in levodopa. Pergolide was well tolerated and resulted in no more withdrawals from therapy than were found in previous trials in younger patients. Compliance with the starter pack was good and permitted a higher dose of pergolide to be achieved. The severity of disease, as measured by the Webster scale, was reduced significantly in both groups ($P < 0.0001$ in tailored regime, $P < 0.005$ in starter pack). Pergolide can be successfully initiated without domperidone in most cases. Pergolide should probably be avoided in patients with pre-existing combined dementia and hallucinosis. The effect on hallucinosis with no dementia was not clarified. Patients can be successfully transferred from bromocriptine or lysuride to pergolide. The conclusion of this study is that pergolide is well tolerated in selected elderly patients with Parkinson's disease. A larger double-blind controlled trial is needed to clarify issues raised in this study.

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on STN DUPLICATE 104

ACCESSION NUMBER: 1998132047 ESBIODBASE

TITLE: Transcranial AC pulsed applications of weak electromagnetic fields reduces freezing and falling in progressive supranuclear palsy: A case report

AUTHOR(S): Sandyk, Reuven

CORPORATE SOURCE: Sandyk, Reuven (Department of Neuroscience, Inst. Biomed. Eng. and Rehab. Serv., Touro College, Dix Hills, NY 11746 (US))

SOURCE: International Journal of Neuroscience (May 1998) Volume 94, Number 1-2, pp. 41-54, 91 refs.
CODEN: IJNUB7 ISSN: 0020-7454

COUNTRY OF PUBLICATION: United Kingdom

DOCUMENT TYPE: Journal; Article

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 31 Jan 2009

Last updated on STN: 31 Jan 2009

AN 1998132047 ESBIODBASE

AB Freezing is a common and disabling symptom in patients with Parkinsonism. It affects most commonly the gait in the form of start hesitation and sudden immobility often resulting in falling. A high incidence of freezing occurs in patients with progressive supranuclear palsy (PSP) which is characterized clinically by a constellation of symptoms including supranuclear ophthalmoplegia, postural instability, axial rigidity, dysarthria, Parkinsonism, and pseudobulbar palsy. Pharmacologic therapy of PSP is currently disappointing and the disease progresses relentlessly to a fatal outcome within the first decade after onset. This report concerns a 67 year old

woman with a diagnosis of PSP in whom freezing and frequent falling were the most disabling symptoms of the disease at the time of presentation. Both symptoms, which were rated 4 on the Unified Parkinson Rating Scale (UPRS) which grades Parkinsonian symptoms and signs from 0 to 4, with 0 being normal and 4 being severe symptoms, were resistant to treatment with dopaminergic drugs such as levodopa, amantadine, selegiline and pergolide mesylate as well as with the potent and highly selective noradrenergic reuptake inhibitor nortriptyline. Weekly transcranial applications of AC pulsed electromagnetic fields (EMFs) of picotesla flux density was associated with approximately 50% reduction in the frequency of freezing and about 80-90% reduction in the frequency of falling after a 6 months follow-up period. At this point freezing was rated 2 while falling received a score of 1 on the UPRS. In addition, this treatment was associated with an improvement in Parkinsonian and pseudobulbar symptoms with the difference between the pre- and post EMF treatment across 13 measures being highly significant ($p < .005$; Sign test). These results suggest that transcranial administration AC pulsed EMFs in the picotesla flux density is efficacious in the treatment of PSP.

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ACCESSION NUMBER: 1998055226 EMBASE
 TITLE: Dopamine: Pharmacologic and therapeutic aspects.
 AUTHOR: Velasco, Manuel (correspondence); Luchsinger, Augusta
 CORPORATE SOURCE: Clinical Pharmacology Unit, Jose M. Vargas Medical School, Universidad Central de Venezuela, Caracas, Venezuela.
 AUTHOR: Velasco, Manuel (correspondence)
 CORPORATE SOURCE: Apdo. P. 76333, El Marques, Caracas 1070A, Caracas, Venezuela.
 AUTHOR: Velasco, Manuel (correspondence)
 CORPORATE SOURCE: Apartado Postal 76333, El Marques, Caracas 1070A, Venezuela
 SOURCE: American Journal of Therapeutics, (Jan 1998) Vol. 5, No. 1, pp. 37-43.
 Refs: 52
 ISSN: 1075-2765 CODEN: AJTHFG
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 20 Mar 1998
 Last Updated on STN: 20 Mar 1998

AB Dopamine is a biogenic amine synthesized in the hypothalamus, in the arcuate nucleus, the caudad, and various areas of the central and peripheral nervous system. It has been widely established that dopamine and its agonists play an important role in cardiovascular, renal, hormonal, and central nervous system regulation through stimulation of alpha and beta adrenergic and dopaminergic receptors. There are several agonists of dopamine-2 (DA(2)) dopaminergic receptors, such as bromocriptine, pergolide, lisuride, quinpirole, and carmoxirole, which inhibit norepinephrine release and produce a decrease in arterial blood pressure; in some cases, bromocriptine and pergolide also reduce heart rate. From a therapeutic point of view, the above-mentioned agonists are used for treating Parkinson's disease, acting over DA(2) dopaminergic receptors of the nigrostriatal system. Bromocriptine and the other dopaminergic agonists mentioned act over DA(2) receptors of the tuberoinfundibular system, inhibiting prolactin release and decreasing hyperprolactinemia and tumor size. Among DA(1) receptor agonists, we can mention fenoldopam, piribedil, ibopamine, SKF 3893, and apomorphine

(nonspecific). Activation of these receptors decreases peripheral resistance, inducing lowering of arterial blood pressure and increases in heart rate, sympathetic tone, and activity of the renin aldosterone system. Among DA(2) receptor antagonists, we can mention metoclopramide, domperidone, sulpiride, and haloperidol. From a therapeutic point of view, metoclopramide and domperidone are used in gastric motility disorders, and haloperidol is used in psychotic alterations. Antagonists of DA(1) receptors are SCH23390 and clozapine. Clozapine is used for treating schizophrenia.

L9 ANSWER 139 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 106

ACCESSION NUMBER: 1998:553159 CAPLUS
DOCUMENT NUMBER: 129:310190
ORIGINAL REFERENCE NO.: 129:63131a,63132a
TITLE: Do dopamine agonists provide neuroprotection?
AUTHOR(S): Yamamoto, Mitsutoshi
CORPORATE SOURCE: Department of Neurology, Kagawa Prefectural Central
Hospital, Takamatsu, 760-8557, Japan
SOURCE: Neurology (1998), 51(Suppl. 2), S10-S12
CODEN: NEURAI; ISSN: 0028-3878
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 33 refs. Many reports provide evidence that certain dopamine (DA) agonists, such as pramipexole or the ergot-derived drugs bromocriptine and pergolide, exhibit neuroprotective effects in in vivo and in vitro expts., whereas other DA agonists are not known to have such effects. The neuroprotective hypothesis for the action of DA agonists is a very attractive working hypothesis, and some of its tenets are derived from the oxidative stress hypothesis for neurodegeneration. If this neuroprotective hypothesis about DA agonists is correct, DA agonist therapy for Parkinson's disease (PD) will become increasingly important. Whereas most neurologists appear to believe that DA agonists have neuroprotective effects, the oxidative stress (free radical) hypothesis, although fascinating, is still controversial. This article reviews exptl. studies on the neuroprotective effects of DA agonists from the clin. standpoint and critical examines the justifications for their clin. use as neuroprotective agents. Studies concerning DA agonist monotherapy, especially de novo treatment studies, provide the most relevant information. Several reports have shown that DA agonists delayed the start of action of levodopa but also have revealed that it was impossible to continue administration of DA agonists alone for long-term treatment of PD. In conclusion, at present there is no clin. evidence that DA agonists have direct neuroprotective effects against PD.

OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 140 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 107

ACCESSION NUMBER: 1998:222857 CAPLUS
DOCUMENT NUMBER: 128:289583
ORIGINAL REFERENCE NO.: 128:57183a,57186a
TITLE: Quinagolide in hyperprolactinemia
AUTHOR(S): Brownell, Judith
CORPORATE SOURCE: Mill Creek, WA, 98012-5811, USA
SOURCE: Reviews in Contemporary Pharmacotherapy (1998), 9(1), 1-75
CODEN: RCPHF; ISSN: 0954-8602
PUBLISHER: Marius Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB Hyperprolactinemia, the most common hypothalamic-pituitary disorder confronting clinicians, is responsible for at least 25% of menstrual cycle disturbances that result in infertility and hypogonadism and up to 60% of cases of galactorrhea. Prolactinomas comprise about 50% of all pituitary adenomas and 12-15% of all intracranial tumors. Most microadenomas (< 10 mm) and nontumoral hyperprolactinemia are found in women, while macroadenomas (> 10 mm) occur equally often in men and women. Macroadenomas may expand, causing neurol. as well as endocrinol. disturbances. The aim of treatment is to lower serum prolactin levels and, if tumor is present, to reduce its size while preserving normal pituitary function. Medical therapy has become the treatment of choice, since the tumor recurrence rate after surgery is relatively high and radiotherapy, the second option, lowers prolactin very slowly and rarely results in normalization. Unique amongst pituitary hormones, normal levels of prolactin are maintained through neg. feedback action of the neurotransmitter dopamine (DA), the hypothalamic prolactin releasing factor. The dopamine D2 receptor on the pituitary lactotroph is specific to prolactin, hence, the use of dopaminomimetic drugs for treatment of hyperprolactinemia. The standard compound and first prolactin-inhibiting drug to be developed was the lysergic acid amide, bromocriptine. Literature reports showed that bromocriptine normalized prolactin levels in a mean 77% of hyperprolactinemic women, restoring menses in 84%. In patients with macroadenomas, normal prolactin levels were reached in an average of 69% and mean tumor shrinkage of > 50% in up to 65% of patients. However, as many as 20% of patients do not tolerate bromocriptine and a comparable percentage are resistant to the drug. Other agents with pharmacol. profiles similar to that of bromocriptine have therefore been introduced. These, also ergot-derived, include pergolide and metergoline representing the clavines, and lisuride and cabergoline of the amino-ergolines. As with bromocriptine, none of the compds. binds with absolute specificity to the dopamine receptor, and most act with similar potency on several other neurotransmitter systems. Quinagolide is a new chemical entity whose design combines the substituted quinoline segment of the ergolines with the linear benzo[g]quinoline segment of the prototypic dopamine agonist, apomorphine. The compound binds directly to the lactotroph D2 receptor, decreasing the synthesis and release of prolactin by reducing its gene transcription through its action on cAMP. Quinagolide showed no action on adrenergic or serotonergic receptors, and its oral and parenteral activity was up to 200-fold that of bromocriptine. The compound is rapidly and well absorbed, extensively metabolized and over 95% excreted in urine and feces. The elimination half-lives of parent drug and metabolites are 22.3 h and 17.5 h, resp. Studies in healthy individuals and in hyperprolactinemic patients showed that maximal prolactin suppression was reached after 2-4 h and that single doses above 0.04 mg suppressed serum prolactin for 24 h. In addition, quinagolide was without neg. effects on other hormones of the pituitary-thyroid, -adrenal, or -gonadal axes, or on growth hormone, and no influence was seen on plasma renin activity or aldosterone levels, both D2 receptor controlled. Double-blind comparison with bromocriptine in 279 hyperprolactinemic women resulted in normoprolactinemia in 66% and 76% of the bromocriptine and quinagolide groups, resp. Regular menses were restored in 82% of the women treated with bromocriptine and in 88% of those treated with quinagolide. Galactorrhea was relieved in 95% of women in both groups. Adverse events were more frequent in the bromocriptine group, accounting for a significantly higher discontinuation rate in these women ($p < 0.01$). A review of quinagolide therapy in 603 women with idiopathic or microadenomatous hyperprolactinemia treated in various series revealed a prolactin normalization rate of 87%. In 92.2% of patients normal menses were restored, and galactorrhea disappeared in 91%. The collective results of treatment with quinagolide in 338 patients with macroadenomas showed that prolactin normalized in 74%; menses were established in 79% of women, and improved libido and sexual function were

achieved in 88% of men. Galactorrhoea ceased in 95% of both male and female patients. Assessment of pituitary imaging showed that the tumors of 73% of the patients decreased in size by a mean 70% during quinagolide treatment, reaching maximal shrinkage within the first 6 mo. In newly-diagnosed patients, maximal size decrease was documented in 76% of the tumors after 2 mo of treatment. Visual field defects normalized in up to 84% of patients. Overall, quinagolide treatment resulted in normoprolactinemia in 53% of bromocriptine-resistant and in 93% of bromocriptine-intolerant patients. Pos. results were reported with the use of quinagolide in nonfunctioning pituitary adenomas, in puerperal lactation inhibition, in patients with acromegaly, and in Parkinson's disease. The major adverse events documented during treatment with quinagolide include nausea, headache, dizziness, and fatigue. The tolerability of the drug was judged by 91% of 670 patients to have been good or very good. Up to 40% of the patients spontaneously reported enhanced well-being. Fewer than 5% discontinued treatment because of adverse events. A review with about 580 refs. No electrocardiogr. or laboratory safety measures were adversely affected by quinagolide treatment. A normalizing trend was apparent in lipid levels and in body wts., particularly in prolactinoma patients with above-normal baseline values. In addition, safety monitoring of quinagolide-induced pregnancies showed that exposure to the drug did not increase the rate of spontaneous abortion, multiple pregnancy, or fetal abnormalities. Review of the pharmacol. and clin. profile of quinagolide demonstrates its considerable advantages as a prolactin-inhibiting agent and allows the conclusion that the compound should be considered as the medical treatment of choice. Its selective D2 binding capacity and lack of ergot structure are apparently responsible for its improved tolerability and greater efficacy in comparison with bromocriptine and related ergot drugs.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 514 THERE ARE 514 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 141 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 108

ACCESSION NUMBER: 1998291263 EMBASE
TITLE: Do dopamine agonists provide neuroprotection?.
AUTHOR: Yamamoto, Mitsutoshi, Dr. (correspondence)
CORPORATE SOURCE: Department of Neurology, Kagawa Prefectural Central Hospital, 5-4-16, Bancho, Takamatsu 760-8557, Japan.
SOURCE: Neurology, (Aug 1998) Vol. 51, No. 2 SUPPL., pp. S10-S12.
Refs: 33
ISSN: 0028-3878 CODEN: NEURAI
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Oct 1998
Last Updated on STN: 1 Oct 1998

AB Many reports provide evidence that certain dopamine (DA) agonists, such as pramipexole or the ergot-derived drugs bromocriptine and pergolide, exhibit neuroprotective effects in in vivo and in vitro experiments, whereas other DA agonists are not known to have such effects. The neuroprotective hypothesis for the action of DA agonists is a very attractive working hypothesis, and some of its tenets are derived from the oxidative stress hypothesis for neurodegeneration. If this

neuroprotective hypothesis about DA agonists is correct, DA agonist therapy for Parkinson's disease (PD) will become increasingly important. Whereas most neurologists appear to believe that DA agonists have neuroprotective effects, the oxidative stress (free radical) hypothesis, although fascinating, is still controversial. This article reviews experimental studies on the neuroprotective effects of DA agonists from the clinical standpoint and critically examines the justifications for their clinical use as neuroprotective agents. Studies concerning DA agonist monotherapy, especially de novo treatment studies, provide the most relevant information. Several reports have shown that DA agonists delayed the start of levodopa but also have revealed that it was impossible to continue administration of DA agonists alone for long-term treatment of PD. In conclusion, at present there is no clinical evidence that DA agonists have direct neuroprotective effects against PD.

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ACCESSION NUMBER: 1999034847 EMBASE
TITLE: [Pergolide].
Pergolide.
AUTHOR: Lledo, A., Dr. (correspondence)
CORPORATE SOURCE: Eli Lilly International Corporation, Lilly Research Centre, 13 Hanover Square, GB-London W1R 0PA, United Kingdom.
SOURCE: Aktuelle Neurologie, (1998) Vol. 25, No. SUPPL. 4, pp. S293-S294.
Refs: 12
ISSN: 0302-4350 CODEN: AKNUAR
COUNTRY: Germany
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: German
SUMMARY LANGUAGE: English; German
ENTRY DATE: Entered STN: 18 Feb 1999
Last Updated on STN: 18 Feb 1999

AB Pergolide is a dopamine agonist with affinity for D1, D2 and D3 receptors. Pergolide has a long half-life, is absorbed rapidly from the gastrointestinal tract, metabolised by the liver and excreted through the kidneys (55%), the faeces (40%) and the lungs (5%). Pergolide has proven to be an efficacious drug in treating Parkinson's disease in several studies. In a large study including 376 patients of pergolide given as concomitant medication to levodopa, a significant increase in motor scores as well as in on-time were reported. Moreover, this motor improvement correlated with an improvement in the activities of daily living. At the same time the levodopa dose could be decreased. In comparative studies against bromocriptine, pergolide has shown to be superior in most cases. Finally, in a recently presented study, pergolide used as a monotherapeutic drug in Parkinson's disease significantly improved UPDRS Part I 'motoricity' and Part II 'activities of daily living'.

L9 ANSWER 143 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 109

ACCESSION NUMBER: 1997:216512 BIOSIS
DOCUMENT NUMBER: PREV199799523016
TITLE: D-1 dopamine receptor activity of anti-Parkinsonian drugs.
AUTHOR(S): Fici, G. J.; Wu, H.; Von Voigtlander, P. F.; Sethy, V. H.
[Reprint author]
CORPORATE SOURCE: CNS Diseases Research, Pharmacia Upjohn Inc., 301 Henrietta

SOURCE: St., Kalamazao, MI 49001, USA
Life Sciences, (1997) Vol. 60, No. 18, pp.
1597-1603.
CODEN: LIFSAK. ISSN: 0024-3205.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 22 May 1997

Last Updated on STN: 22 May 1997

AB Clinical and preclinical investigations suggest that stimulation of D-1 dopamine receptors may be responsible for dyskinesias induced by dopamine agonist treatment of Parkinson's Disease (PD), and that these dyskinesias may be decreased by treatment with a D-1 antagonist (clozapine). Therefore, the effects of dopamine agonists and antagonists have been investigated in a primary cerebellar granule cell model of cAMP formation that seems to be highly responsive to the D-1 receptors. SKF 38393, lisuride, apomorphine, pergolide, dopamine, bromocriptine and 7-OH-DPAT showed concentration-dependent increases in cAMP formation, with EC-50 S (in μ -M) of 0.013, 0.053, 0.25, 1.04, 2.18, 50.9 and 54.4, respectively. SKF 38393, apomorphine, dopamine and pergolide had similar intrinsic activity (100%), while the intrinsic activities of 7-OH-DPAT, bromocriptine and lisuride were 28.0%, 20.7% and 17.2%, respectively. SCH 23390, a selective D-1 dopamine receptor antagonist, blocked an increase in cAMP formation produced by EC-50 concentrations of all of the dopamine agonists investigated in this study. Clozapine concentration-dependently blocked pergolide-induced increases in cAMP and was approx 1700-fold less potent than SCH 23390 (IC-50: 0.97 μ -M and 0.56 nM, respectively). U-95666A (1-1000 μ -M), selective for the D-2 receptors, showed no significant effect on cAMP, while pramipexole (0.1-100 μ -M), a D-3 preferring agonist, did not elevate cAMP. These data suggest that primary cerebellar granule cell cultures are an excellent model for measuring D-1 dopamine receptor-mediated changes in cellular cAMP. The results are discussed with reference to the relationship between the D-1 receptor-stimulated increase in cAMP formation and the induction of dyskinesia in humans by these anti-parkinsonian drugs.

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ACCESSION NUMBER: 1997273389 EMBASE

TITLE: [Comparative study of effects of bromocriptine and pergolide in Parkinson's disease].
Estudio comparativo del efecto de la bromocriptina y el pergolide en la enfermedad de parkinson.

AUTHOR: de Yebenes, J.G., Dr. (correspondence); Garcia-Ruiz, P.J.; Sanchez-Pernaute, R.

CORPORATE SOURCE: Servicio de Neurologia, Fundacion Jimenez Diaz, Madrid, Spain.

AUTHOR: de Yebenes, J.G., Dr. (correspondence)

CORPORATE SOURCE: Servicio de Neurologia, Fundacion Jimenez Diaz, Ciudad Universitaria, Avda Reyes Catolicos 2, E-28040 Madrid, Spain.

SOURCE: Revista de Neurologia, (Sep 1997) Vol. 25, No. 145, pp. 1343-1345.

Refs: 26

ISSN: 0210-0010 CODEN: RVNRAA

COUNTRY: Spain

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 037 Drug Literature Index

038 Adverse Reactions Titles

008 Neurology and Neurosurgery

LANGUAGE: Spanish; Castilian

SUMMARY LANGUAGE: English; Spanish; Castilian

ENTRY DATE: Entered STN: 2 Oct 1997

Last Updated on STN: 2 Oct 1997

AB Introduction. Bromocriptine and pergolide are the two dopamine agonists most often used in Parkinson's disease. Few comparative studies of the efficacy of both compounds are available. Objective. To compare the relative efficacy of bromocriptine and pergolide in patients with Parkinson's disease and intermediate stages of evolution. Methods. Open label study of 5-months of duration. The first agonist was given for two months and after a period of substitution of one month, the second agonist was also maintained for two months. Results. Pergolide was more effective than bromocriptine for global scores of the UPDRS, total motor scores. Clinical symptoms, akinesia and rigidity. Both compounds were equal effective for the treatment of tremor and fluctuations. Both agonists produced similar side effects. Conclusions. At the ratio 1/10 mg/day pergolide was more effective than bromocriptine in patients with Parkinson's disease at intermediate stages of evolution.

L9 ANSWER 145 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 111

ACCESSION NUMBER: 1997:403852 BIOSIS

DOCUMENT NUMBER: PREV199799710055

TITLE: U-95666E: A potential anti-Parkinsonian drug with anxiolytic activity.

AUTHOR(S): Sethy, Vimala H. [Reprint author]; Ellerbrock, Brenda R.; Wu, Haiyan

CORPORATE SOURCE: CNS Diseases Res., 7251-209-508, Pharmacia and Upjohn, Inc., 301 Henrietta St., Kalamazoo, MI, USA

SOURCE: Progress in Neuro-Psychopharmacology and Biological Psychiatry, (1997) Vol. 21, No. 5, pp. 873-883. CODEN: PNPPD7. ISSN: 0278-5846.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 24 Sep 1997

Last Updated on STN: 24 Sep 1997

AB 1. U-95666E, a D-2 selective dopamine agonist, was investigated for its effect on rat striatal acetylcholine (ACh) concentration and the results were compared with those obtained with pergolide, pramipexole and bromocriptine under similar conditions. 2. U-95666E, pergolide, pramipexole and bromocriptine dose-dependently increased striatal ACh concentration both in the non-reserpinized and reserpinized rats. 3. Intrinsic activity of U-95666E was similar to pergolide and pramipexole in non-reserpinized rats, but significantly lower in reserpinized rats. 4. The sensitivity of these dopamine agonists for increasing ACh levels in the denervated as compared to innervated striatum were significantly (p lt 0.01) higher. 5. U-95666E also has anxiolytic activity in mice. 6. In conclusion, U-95666E may have potential for the treatment of Parkinson's Disease and associated anxiety.

L9 ANSWER 146 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 112

ACCESSION NUMBER: 1997:422228 CAPLUS

DOCUMENT NUMBER: 127:103729

ORIGINAL REFERENCE NO.: 127:19807a,19810a

TITLE: Pharmacologic options for managing Parkinson's disease

AUTHOR(S): Evidente, Virgillo G. H.; Adler, Charles H.

CORPORATE SOURCE: Mayo Clinic, Scottsdale, AZ, USA

SOURCE: Formulary (1997), 32(6), 594-596, 601-602, 604, 607-610

CODEN: FORMF9; ISSN: 1082-801X

PUBLISHER: Advanstar

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 54 refs. Current therapy for idiopathic Parkinson's disease (IPD) is mainly symptomatic with the focus on individualizing therapy for early and advanced stage disease. The most effective drug for both early and advanced IPD is levodopa. For patients with mild disease and minimal disability, monotherapy with anticholinergic agents, amantadine, selegiline, or dopamine agonists (eg, bromocriptine and pergolide) may be useful. Advanced disease is usually associated with levodopa-induced complications, such as motor fluctuations and dyskinesias, which may be alleviated by adjusting levodopa dosing or by adding a dopamine agonist. Although no drug has been unequivocally proven to be neuroprotective in IPD, selegiline, amantadine, bromocriptine, and pergolide may play some role in delaying the progression of disease.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 147 OF 331 MEDLINE on STN

ACCESSION NUMBER: 1998007034 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9446045

TITLE: [Dopamine agonist in the treatment of Parkinson's disease].
Agonisci dopaminy w leczeniu choroby Parkinsona.

AUTHOR: Kuran W

CORPORATE SOURCE: I Kliniki Neurologicznej IPiN w Warszawie.

SOURCE: Neurologia i neurochirurgia polska, (1997 May-Jun)

Vol. 31, No. 3, pp. 545-54. Ref: 40

Journal code: 0101265. ISSN: 0028-3843.

PUB. COUNTRY: Poland

DOCUMENT TYPE: (ENGLISH ABSTRACT)

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

LANGUAGE: Polish

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199801

ENTRY DATE: Entered STN: 6 Feb 1998

Last Updated on STN: 6 Feb 1998

Entered Medline: 27 Jan 1998

AB In the review paper is discussed the group of dopamine agonists which act directly on the postsynaptic receptors in the striatum, and have been used since over 20 years in the treatment of various stages of Parkinson's disease. For practical reasons they are divided in the paper into three groups: drugs used formerly and now gradually withdrawn mainly because of various adverse effects, new drugs whose effectiveness and usefulness have not yet been confirmed clinically, and three drugs (bromocriptine, lisuride, pergolide) used fairly widely with clinically confirmed effectiveness. The mechanism of their action and clinical results are described.

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ACCESSION NUMBER: 1998001191 EMBASE

TITLE: A review of the efficacy of the dopamine agonists pergolide and bromocriptine in the treatment of Parkinson's disease.

AUTHOR: Nohria, V. (correspondence)

CORPORATE SOURCE: Department of Neurology, Division of Pediatric Neurology,
Univ. of Virginia School of Medicine, Charlottesville, VA,
United States.

AUTHOR: Partiot, A.

CORPORATE SOURCE: Lilly France S.A., 203 Bureaux De La Colline, 92213

Saint-Cloud, France.
AUTHOR: Nohria, V. (correspondence)
CORPORATE SOURCE: Department of Neurology, Division of Pediatric Neurology,
University Virginia School Medicine, Charlottesville, VA.
SOURCE: European Journal of Neurology, (1997) Vol. 4, No.
6, pp. 537-543.
Refs: 25
ISSN: 1351-5101 CODEN: EJNEFL
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
006 Internal Medicine
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Jan 1998
Last Updated on STN: 20 Jan 1998

AB This review summarizes those studies, completed over the last 15 years, which compare the clinical benefit of the two most commonly used dopamine agonists, pergolide and bromocriptine. In these studies, both drugs were evaluated as adjunctive therapy to levodopa for the treatment of Parkinson's disease (PD). Ten studies are analyzed and the affect of pergolide and bromocriptine on PD compared. Although variation in study design and disease rating scales prevents the opportunity for a true meta-analysis, this review analyses the outcome of each individual study to assess the benefit of pergolide over bromocriptine. Pergolide improves patients' activities-of-daily-living and their clinical PD symptoms over bromocriptine. Additionally, a large percentage of patients who do not respond to bromocriptine, or whose PD symptoms worsened, improved on pergolide. Furthermore, patients who are adequately treated with bromocriptine experienced additional improvement with pergolide therapy. In summary, pergolide provided benefits to PD patients over bromocriptine in nine studies and was equivalent in the tenth. The benefits associated with pergolide may be partly due to the action of pergolide on dopamine D(1) and D(2) receptors (bromocriptine is associated with the D(2) agonism). In conclusion, in the majority of completed studies to date, pergolide provided greater improvement to the clinical signs and symptoms of PD than bromocriptine.

L9 ANSWER 149 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 114
ACCESSION NUMBER: 1997:282730 CAPLUS
DOCUMENT NUMBER: 126:324698
ORIGINAL REFERENCE NO.: 126:62895a,62898a
TITLE: Pergolide: a review of its pharmacology and
therapeutic use in Parkinson's disease
AUTHOR(S): Markham, Anthony; Benfield, Paul
CORPORATE SOURCE: Adis International Limited, Auckland, N. Z.
SOURCE: CNS Drugs (1997), 7(4), 328-340
CODEN: CNDREF; ISSN: 1172-7047
PUBLISHER: Adis
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 71 refs. The semisynthetic ergoline dopamine agonist pergolide has demonstrated activity at pre- and postsynaptic dopamine D2 receptors in in vitro and in vivo animal studies. However, unlike other dopamine agonists such as bromocriptine, pergolide also has agonist activity at dopamine D1 receptors. Certain other pharmacol. effects of pergolide, such as reduction of dopamine turnover and effects on free radical scavenging enzymes, may be relevant in the early treatment of Parkinson's disease but this has not

been conclusively determined. Short and long term noncomparative studies show that pergolide is an effective adjunct to levodopa therapy in patients with advancing Parkinson's disease, reducing the adverse effects of long term levodopa monotherapy and often enabling a reduction in levodopa dosage. In placebo comparisons pergolide was generally more effective than placebo and was associated with benefits similar to those seen in noncomparative studies. Longitudinal comparisons in individual patients indicate that the antiparkinsonian efficacy of pergolide is similar to that of mesulergine, lergotril and lisuride, and may be superior to that of bromocriptine. Controlled comparisons with bromocriptine tend to support this latter finding. Studies evaluating the efficacy of pergolide as monotherapy early in the course of Parkinson's disease have shown the drug to be effective, but opinion is divided as to the value of early treatment with dopamine agonists (as opposed to levodopa monotherapy). Thus, pergolide is an effective adjunct to levodopa therapy in patients with advanced Parkinson's disease and may have a role in the treatment of early disease if its postulated beneficial effects on disease progression are proven. Pergolide is a semisynthetic ergoline dopamine agonist used in the treatment of Parkinson's disease. It has potent activity at presynaptic dopamine D2 receptors but is also active at postsynaptic D2 and dopamine D1 receptors. In vitro, pergolide suppressed D2-mediated prolactin release from rat anterior pituitary fragments and inhibited potassium-mediated dopamine or acetylcholine release from rat caudate slices. Pergolide-induced activation of rat striatal D1 receptors has been shown to stimulate adenylate cyclase activity which, in turn, increased production of cAMP. The majority of receptor binding studies indicate that pergolide is considerably more selective for D2 than for D1 receptors. In vivo, pergolide has been shown to induce contralateral turning in rats with right-side nigrostriatal lesions; it also induced climbing in rats selected on the basis of a climbing response to apomorphine. Pergolide had similar actions to those of selective D2 agonists in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced hemiparkinsonian monkeys but was more potent than selective D1 agonists. Pergolide improved parkinsonian symptoms in another study in this model. Its effects were more marked, but of shorter duration, than those of bromocriptine or cabergoline. One theory regarding the cause of Parkinson's disease is that metabolism of dopamine produces free radicals which damage nigral neurons. Its effects on oxygen radical scavenging enzymes are unclear; the drug induced superoxide dismutase in one in vivo animal study but had no effect in another (but did induce catalase and glutathione peroxidase). Single 1, 2, 5 and 10mg doses of pergolide produced mean peak plasma concns. (Cmax) of 2.09, 4.57, 20.3 and 26 µg/L, resp., in rhesus monkeys (administration of therapeutic doses to volunteers was considered unethical). The time to Cmax ranged between 2.4 and 2.7 h at all dose levels. Mean steady-state pergolide plasma concns. of 0.0275 to 1.167 µg/L were recorded during treatment with pergolide 2.25 to 9 mg/day in patients with Parkinson's disease; extensive interpatient variability was noted. 55% Of a 0.138mg radiolabeled oral dose of pergolide was excreted in the urine of volunteers; a further 40 to 50% of radioactivity appeared in the feces and approx. 3% appeared in expired air.

OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)

L9 ANSWER 150 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 115

ACCESSION NUMBER: 1997:308593 BIOSIS

DOCUMENT NUMBER: PREV199799616396

TITLE: Improvement of motor fluctuations in patients with

Parkinson's Disease following treatment with high doses of pergolide and cessation of Levodopa.
AUTHOR(S): Schwarz, Johannes [Reprint author]; Scheidtmann, Klaus; Trenkwalder, Claudia
CORPORATE SOURCE: Dep. Neurol., RKU, Univ. Ulm, Oberer Eselsberg 45, D-89081 Ulm, Germany
SOURCE: European Neurology, (1997) Vol. 37, No. 4, pp. 236-238.
CODEN: EUNEAP. ISSN: 0014-3022.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jul 1997
Last Updated on STN: 26 Jul 1997

AB The combination of levodopa and a dopamine agonist in the treatment of patients with Parkinson's disease often reduces the severity of motor fluctuations. In patients with very severe motor fluctuations, monotherapy with continuous subcutaneous infusions of the dopamine agonist apomorphine may result in a marked reduction of hyperkinesia and on-off phenomena. We report 3 patients with Parkinson's disease and motor fluctuations who received high doses of pergolide without levodopa resulting in a reduction of motor fluctuations. All patients received doses of pergolide exceeding the maximum recommended dose. One patient also required additional therapy with amantadine. These data show that in some patients oral treatment with high doses of a dopamine agonist may improve the severity of motor fluctuations and achieve a good control of parkinsonian signs without concomitant levodopa treatment.

L9 ANSWER 151 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1997:836 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 34-11266
TITLE: Drug treatment of Parkinson's disease in the 1990s: achievements and future possibilities
AUTHOR(S): Hughes, A. J.
CORPORATE SOURCE: Neurol. Dept., Austin and Repatriation Med. Ctr., Repatriation Campus, Banksia St., West Heidelberg, VIC 3081, Australia
SOURCE: Drugs (New Zealand), (Feb 1997) Vol. 53, pp. 195-205. 65 Refs.
CODEN: DRUGAY. ISSN: 0012-6667.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 97:3096
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB Advances in the medical treatment of Parkinson disease, current therapies with levodopa, bromocriptine, pergolide, selegiline, amantadine, and anticholinergic agents, and the management of drug induced dyskinesias are discussed.
Rosemary Gregor

L9 ANSWER 152 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 116

ACCESSION NUMBER: 1998003083 EMBASE
TITLE: New options for treatment of Parkinson's disease.
AUTHOR: Lewitt, P.A., Dr. (correspondence)
CORPORATE SOURCE: Clinical Neuroscience Center, 5821 West Maple Road, West Bloomfield, MI 48322, United States.
SOURCE: Bailliere's Clinical Neurology, (1997) Vol. 6, No. 1, pp. 109-123.

Refs: 66
ISSN: 0961-0421 CODEN: BCNUEK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 22 Jan 1998
Last Updated on STN: 22 Jan 1998

AB New medications recently developed for treating Parkinson's disease include two inhibitors of catechol-O-methyltransferase (COMT), entacapone and tolcapone, which, by decreasing the elimination of levodopa, extend the duration of its effects. Increased 'on' time and less 'wearing-off' symptomatology can be expected with the use of these COMT inhibitors. Two non-ergot dopaminergic agonists (pramipexole and ropinirole) and a long-acting ergoline (cabergoline) are also being introduced. These dopaminergic agonists, like the ergot derivatives currently available (bromocriptine, lisuride, and pergolide), are useful as adjuncts to levodopa, and are also efficacious as monotherapies.

L9 ANSWER 153 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 117
ACCESSION NUMBER: 1997:80152 CAPLUS
DOCUMENT NUMBER: 126:75118
ORIGINAL REFERENCE NO.: 126:14545a,14548a
TITLE: Integration of a Highly Selective Demethylation of a Quaternized Ergoline into a One-Pot Synthesis of Pergolide
AUTHOR(S): Misner, Jerry W.; Kennedy, Joseph H.; Biggs, W. Scott
CORPORATE SOURCE: Chemical Process Research and Development Division, Lilly Research Laboratories, Indianapolis, IN, 46285-4813, USA
SOURCE: Organic Process Research & Development (1997), 1(1), 77-80
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 126:75118

AB A high-yielding one-pot synthesis of pergolide, an alkaloid useful for the adjunctive treatment of Parkinson's disease, starting from dihydrolyzergol was described. The process involved the formation of quaternized amine intermediates, followed by a highly selective demethylation and thioether formation via thiomethoxide ion. A novel tandem chromatog. procedure was used to remove closely related byproducts, which included an unexpected and unusual thiomethyl ether homolog of pergolide.

OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 154 OF 331 MEDLINE on STN DUPLICATE 118
ACCESSION NUMBER: 1997431196 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9285289
TITLE: Treatment with weak electromagnetic fields restores dream recall in a parkinsonian patient.
AUTHOR: Sandyk R
CORPORATE SOURCE: Department of Neuroscience, Institute for Biomedical Engineering and Rehabilitation Services, Touro College, Dix Hills, NY 11746, USA.

SOURCE: The International journal of neuroscience, (1997 Jun) Vol. 90, No. 1-2, pp. 75-86.
Journal code: 0270707. ISSN: 0020-7454.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 5 Nov 1997
Last Updated on STN: 5 Nov 1997
Entered Medline: 23 Oct 1997

AB Absent or markedly reduced REM sleep with cessation of dream recall has been documented in numerous neurological disorders associated with subcortical dementia including Parkinson's disease, progressive supranuclear palsy and Huntington's chorea. This report concerns a 69 year old Parkinsonian patient who experienced complete cessation of dreaming since the onset of motor disability 13 years ago. Long term treatment with levodopa and dopamine (DA) receptor agonists (bromocriptine and pergolide mesylate) did not affect dream recall. However, dreaming was restored after the patient received three treatment sessions with AC pulsed picotesla range electromagnetic fields (EMFs) applied extracranially over three successive days. Six months later, during which time the patient received 3 additional treatment sessions with EMFs, he reported dreaming vividly with intense colored visual imagery almost every night with some of the dreams having sexual content. In addition, he began to experience hypnagogic imagery prior to the onset of sleep. Cessation of dream recall has been associated with right hemispheric dysfunction and its restoration by treatment with EMFs points to right hemispheric activation, which is supported by improvement in this patient's visual memory known to be subserved by the right temporal lobe. Moreover, since DA neurons activate REM sleep mechanisms and facilitate dream recall, it appears that application of EMFs enhanced DA activity in the mesolimbic system which has been implicated in dream recall. Also, since administration of pineal melatonin has been reported to induce vivid dreams with intense colored visual imagery in normal subjects and narcoleptic patients, it is suggested that enhanced nocturnal melatonin secretion was associated with restoration of dream recall in this patient. These findings demonstrate that unlike chronic levodopa therapy, intermittent pulsed applications of AC picotesla EMFs may induce in Parkinsonism reactivation of reticular-limbic-pineal systems involved in the generation of dreaming.

L9 ANSWER 155 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 119
ACCESSION NUMBER: 1997:80086 CAPLUS
DOCUMENT NUMBER: 126:75111
ORIGINAL REFERENCE NO.: 126:14545a,14548a
TITLE: HPLC Purification of Pergolide Using Silica Gel
AUTHOR(S): Kennedy, Joseph H.
CORPORATE SOURCE: Lilly Research Laboratories, Division of Eli Lilly and Company, Indianapolis, IN, 46285, USA
SOURCE: Organic Process Research & Development (1997), 1(1), 68-71
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pergolide is a synthetic ergot alkaloid approved for the treatment of Parkinson's disease. Process-related impurities from the synthesis are difficult to remove chemical without significant yield loss. An alternative purification procedure was necessary. Pergolide is soluble in nonaq. solvents such as chloroform, methylene chloride, and

DMF. Solubility is improved when the halocarbon is mixed with an alc. such as methanol. These characteristics are desirable for silica gel chromatog. This paper describes the evaluation of solubility as a function of halocarbon and the development of a silica gel system to sep. the process-related impurities from pergolide. The criteria for choosing a com. available silica gel and results from purification using axial compression column technol. are also discussed.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD
(3 CITINGS)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 156 OF 331 Elsevier Biobase COPYRIGHT 2009 Elsevier Science B.V.
on STN DUPLICATE 120

ACCESSION NUMBER: 1998069290 ESBIODASE
TITLE: Speech impairment in Parkinson's disease is improved by
transcranial application of electromagnetic fields
AUTHOR(S): Sandyk, Reuven
CORPORATE SOURCE: Sandyk, Reuven (Department of Neuroscience, Institute
for Biomedical Engineering, Rehab. Services of Touro
College, Dix Hills, NY 11746 (US))
SOURCE: International Journal of Neuroscience (Nov
1997) Volume 92, Number 1-2, pp. 63-72, 59 refs.
CODEN: IJNUB7 ISSN: 0020-7454
COUNTRY OF PUBLICATION: United Kingdom
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jan 2009
Last updated on STN: 31 Jan 2009

AN 1998069290 ESBIODASE

AB A 52 year old fully medicated physician with juvenile onset
Parkinsonism experienced 4 years ago severe 'on-off'
fluctuations in motor disability and debilitating speech impairment with
severe stuttering which occurred predominantly during 'on-off' periods.
His speech impairment improved 20%-30% when sertraline (75 mg/day), a
serotonin reuptake inhibitor, was added to his dopaminergic medications
which included levodopa, amantadine, selegiline and pergolide
mesylate. A more dramatic and consistent improvement in his speech
occurred over the past 4 years during which time the patient received,
on a fairly regular basis, weekly transcranial treatments with AC pulsed
electromagnetic fields (EMFs) of picotesla flux density. Recurrence of
speech impairment was observed on several occasions when regular
treatments with EMFs were temporarily discontinued. These findings
demonstrate that AC pulsed applications of picotesla flux density EMFs
may offer a nonpharmacologic approach to the management of speech
disturbances in Parkinsonism. Furthermore, this case
implicates cerebral serotonergic deficiency in the pathogenesis of
Parkinsonian speech impairment which affects more than 50% of
patients. It is believed that pulsed applications of EMFs improved this
patient's speech impairment through the facilitation of serotonergic
transmission which may have occurred in part through a synergistic
interaction with sertraline.

L9 ANSWER 157 OF 331 MEDLINE on STN DUPLICATE 121

ACCESSION NUMBER: 1997166726 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9014424
TITLE: Treatment of Parkinson's disease with multiple drugs.
AUTHOR: Kuno S
CORPORATE SOURCE: Department of Neurology, Utano National Hospital.
SOURCE: Nippon rinsho. Japanese journal of clinical medicine,
(1997 Jan) Vol. 55, No. 1, pp. 59-64. Ref: 9

Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 7 Apr 1997
Last Updated on STN: 7 Apr 1997
Entered Medline: 26 Mar 1997

AB All major symptoms of Parkinson's disease, i.e., rigidity, tremor, hypokinesia and postural instability are induced by an impaired dopaminergic neurotransmission in the nigro-striatal pathway. Levodopa pioneered the symptomatic therapy of Parkinson's disease. While it is effective on the motor symptoms, long-term levodopa therapy often results in dyskinesia, motor fluctuations and psychosis. Coadministration of levodopa and dopamine agonists, bromocriptine and pergolide, decreases these adverse side effects. Anticholinergics and amantadine are often effective as adjuvant drugs for the early stage of patients with Parkinson's disease. Furthermore, L-threo-DOPS, nor-adrenergic precursor drug, is sometimes effective for the advanced stage of Parkinson's disease. Thus coadministration of multiple antiparkinsonian drugs, rather than single therapy of levodopa, is useful for the long-term treatment of Parkinson's disease.

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STN DUPLICATE 122

ACCESSION NUMBER: 1997:214715 BIOSIS
DOCUMENT NUMBER: PREV199799521219
TITLE: New strategies with dopaminergic drugs: Modified formulations of levodopa and novel agonists.
AUTHOR(S): Goetz, Christopher G.
CORPORATE SOURCE: Rush Univ./Rush-Presbyterian-St. Luke's Med. Cent., Chicago, IL 60612, USA
SOURCE: Experimental Neurology, (1997) Vol. 144, No. 1, pp. 17-20.
CODEN: EXNEAC. ISSN: 0014-4886.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 22 May 1997
Last Updated on STN: 22 May 1997

AB Most new pharmacological therapies in Parkinson's disease focus on the dopaminergic system. Drugs that enhance dopaminergic function fall into three primary categories: amino acid precursors to dopamine, agonists that stimulate dopamine receptors, and enzyme antagonists that prevent the metabolism of dopamine and hence permit more or prolonged neurotransmitter activity; the first two are discussed below. Within the first category, levodopa is the amino acid precursor to dopamine, and a number of modifications in its formulation have been developed to enhance dopaminergic activity. In the area of agonists, new agents pramipexole, ropinerole, and cabergoline have recently been developed to complement the currently available bromocriptine and pergolide, and these new drugs maybe released in the United States.

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ACCESSION NUMBER: 1998222085 EMBASE
TITLE: Is stereotactic surgical treatment still necessary for Parkinson's disease in the contemporary trend of medical therapy with dopamine receptor agonist?.

AUTHOR: Amano, Keiichi, Dr. (correspondence); Takakura, Kintomo
CORPORATE SOURCE: Department of Neurosurgery, Neurological Institute, Tokyo
Women's Medical College, 8-1 Kawada-cho, Sinjyuku-ku, Tokyo
162, Japan.
SOURCE: Stereotactic and Functional Neurosurgery, (1997)
Vol. 69, No. 1-4, pp. 5-18.
Refs: 10
ISSN: 1011-6125 CODEN: SFUNE4
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 1998
Last Updated on STN: 6 Aug 1998

AB Clinical experience with the use of pergolide is presented in 55 patients with Parkinson's disease. Fifty to 900 µg/day (mean 242.73, SD 217.51) of pergolide and 0.64-1.05 µg/kg/day (mean 4.58, SD 4.25) pergolide was given together with L-carbidopa to 29 males and 26 females for a period of up to 2 years 7 months. Low-dose pergolide together with L-carbidopa is effective in the treatment of parkinsonism without side effects, even in advanced stages of the disease. No patients required surgical treatment such as pallidotomy or deep brain stimulation recommended by other investigators. We emphasize that parkinsonism can be sufficiently treated with pergolide and L-dopa and that surgical treatment should be minimized unless there is no alternative.

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ACCESSION NUMBER: 1997280832 EMBASE
TITLE: Pergolide: An effective antiparkinsonian agent.
SOURCE: Drugs and Therapy Perspectives, (1997) Vol. 10,
No. 6, pp. 1-5.
Refs: 11
ISSN: 1172-0360 CODEN: DTHPEE
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 2 Oct 1997
Last Updated on STN: 2 Oct 1997

AB The dopamine agonist pergolide is an effective adjunct to levodopa in patients with advancing Parkinson's disease. Pergolide reduces the motor complications of long-term levodopa monotherapy and often enables a reduction in the dosage of levodopa in patients with Parkinson's disease. Pergolide appears to have similar efficacy and tolerability to other dopamine agonists, although some clinical data indicate that pergolide is a more effective adjunct to levodopa than bromocriptine. Monotherapy with pergolide has also proven effective in improving symptoms in patients with early Parkinson's disease. However, compared with levodopa in this indication the value of pergolide monotherapy remains unclear. Pergolide therapy should be introduced and discontinued gradually in order to minimise adverse effects.

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ACCESSION NUMBER: 1997187973 EMBASE
TITLE: Pharmacologic options for managing Parkinson's disease.
AUTHOR: Evidente, Virgilio G. H.
CORPORATE SOURCE: Mayo Clinic, Scottsdale, AZ, United States.
AUTHOR: Adler, Charles H., Dr. (correspondence)
CORPORATE SOURCE: Parkinson's Dis. Movement Disord. C., Department of
Neurology, Mayo Clinic, Scottsdale, AZ, United States.
AUTHOR: Adler, Charles H., Dr. (correspondence)
CORPORATE SOURCE: Department of Neurology, Mayo Clinic Scottsdale, 13400 Shea
Blvd., Scottsdale, AZ 85259, United States.
SOURCE: Formulary, (Jun 1997) Vol. 32, No. 6, pp.
594-596+601-602+604+607-610.
Refs: 54
ISSN: 0098-6909 CODEN: FORMF9
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jul 1997
Last Updated on STN: 31 Jul 1997

AB Current therapy for idiopathic Parkinson's disease (IPD) is mainly symptomatic with the focus on individualizing therapy for early and advanced stage disease. The most effective drug for both early and advanced IPD is levodopa. For patients with mild disease and minimal disability, monotherapy with anticholinergic agents, amantadine, selegiline, or dopamine agonists (eg, bromocriptine and pergolide) may be useful. Advanced disease is usually associated with levodopa-induced complications, such as motor fluctuations and dyskinesias, which may be alleviated by adjusting levodopa dosing or by adding a dopamine agonist. Although no drug has been unequivocally proven to be neuroprotective in IPD, selegiline, amantadine, bromocriptine, and pergolide may play some role in delaying the progression of disease.

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STN DUPLICATE 124

ACCESSION NUMBER: 1996:540851 BIOSIS
DOCUMENT NUMBER: PREV199699263207
TITLE: Scavenging effects of dopamine agonists on nitric oxide radicals.
AUTHOR(S): Nishibayashi, Sakiko; Asanuma, Masato; Kohno, Masahiro;
Gomez-Vargas, Marvin; Ogawa, Norio [Reprint author]
CORPORATE SOURCE: Dep. Neurosci., Inst. Molecular Cellular Med., Okayama
Univ. Med. Sch., 2-5-1 Shikatacho, Okayama 700, Japan
SOURCE: Journal of Neurochemistry, (1996) Vol. 67, No. 5,
pp. 2208-2211.
CODEN: JONRA9. ISSN: 0022-3042.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1996
Last Updated on STN: 10 Dec 1996

AB It has recently been considered that free radicals are closely involved in the pathogenesis of Parkinson's disease (PD), and the level of nitric oxide radical (.NO), one of the free radicals, is reported to increase in PD brain. In the present study, we established a direct detection system for .NO in an in vitro .NO-generating system using 3-(2-hydroxy-1-methylethyl-2-nitrosohydrazino)-N-methyl-1-propanamine as an .NO donor and 2-(4-carboxyphenyl)-4,4,5,5-tetramethylimidazoline-1-oxyl 3-oxide (carboxy-PTIO) by electron spin resonance (ESR) spectrometry and

examined the quenching effects of the dopamine agonists pergolide and bromocriptine on the amount of .NO generated. .NO appeared to be scavenged by pergolide and, to a lesser extent, by bromocriptine. In the competition assay, the 50% inhibitory concentration values for pergolide and bromocriptine were estimated to be approx 23 and 200 μ M, respectively. It was previously reported that in vivo treatment of pergolide and bromocriptine completely protected against the decrease in levels of striatal dopamine and its metabolites in the 6-hydroxydopamine-injected mouse. Considering these findings, pergolide and probably bromocriptine may also protect against dysfunction of dopaminergic neurons because of its multiple effects; not only does it stimulate the presynaptic autoreceptors, but it also directly scavenges .NO radicals and hence protects against .NO-related cytotoxicity. This ESR spectrometry method using carboxy-PTIO may be useful for screening other drugs that can quench .NO.

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ACCESSION NUMBER: 1997:77756 BIOSIS
DOCUMENT NUMBER: PREV199799384459
TITLE: Effect of cabergoline, a long-acting dopamine D-2 agonist, on reserpine-treated rodents.
AUTHOR(S): Miyagi, Masaharu,; Arai, Nobuhiko; Taya, Fumie; Itoh, Fumiaki; Komatsu, Yoshimitsu; Kojima, Masami [Reprint author]; Isaji, Masayuki
CORPORATE SOURCE: Pharmacological Lab., Kissei Pharmaceutical Co. Ltd., 4365-1 Kashiwabara, Hotaka, Nagano 399-83, Japan
SOURCE: Biological and Pharmaceutical Bulletin, (1996) Vol. 19, No. 11, pp. 1499-1502.
ISSN: 0918-6158.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Feb 1997
Last Updated on STN: 26 Feb 1997

AB We studied the characterization of cabergoline, a new ergot alkaloid derivative and a selective dopamine D-2 receptor agonist, in comparison to bromocriptine and pergolide in reserpine-treated rodents. Cabergoline (0.25-1.0 mg/kg, s.c.) improved dose-dependently the reserpine-induced akinesia that was assessed on the locomotor activity, and the efficacy lasted longer than those of bromocriptine (1.2-5.0 mg/kg, s.c.) or pergolide (0.0625-0.5 mg/kg, s.c.). Cabergoline (ED-50 = 1.10 mg/kg, at 4 h after the administration of drugs) also reversed catalepsy, the failure to correct an externally imposed posture, and its efficacy was stronger and longer than bromocriptine (ED-50 = 4.65 mg/kg, at 4 h). Further, reserpine-induced rigidity was improved equally by cabergoline (0.125-1.0 mg/kg, i.v.) and bromocriptine (1.0 mg/kg, i.v.). When cabergoline was administered together with 3-(3,4-dihydroxyphenyl)-L-alanine (L-DOPA), the effects were additive. Our results indicate that the long-lasting effects of cabergoline could be beneficial for treating Parkinson's disease.

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ACCESSION NUMBER: 1996356366 EMBASE
TITLE: Improvement of ophthalmoplegia by 5-hydroxytryptophan in two cases of progressive supranuclear palsy.
AUTHOR: Yukitake, Motohiro, Dr. (correspondence); Takashima, Yuki; Kurohara, Kazuhiro; Matsui, Makoto; Kuroda, Yasuo
CORPORATE SOURCE: Division of Neurology, Department of Internal Medicine, Saga Medical School, Saga, Japan.
SOURCE: Clinical Neurology, (Jul 1996) Vol. 36, No. 7, pp. 906-908.

Refs: 7
ISSN: 0009-918X CODEN: RISHDJ
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
ENTRY DATE: Entered STN: 18 Dec 1996
Last Updated on STN: 18 Dec 1996

AB We report two patients with clinically diagnosed progressive supranuclear palsy (PSP): a 69-year-old man and a 73-year-old woman. Both patients showed supranuclear ophthalmoplegia, postural instability, pseudobulbar palsy, and Parkinsonism. In the first patient, we administered L-dopa/carbidopa (300mg/30mg/day), which moderately improved gait disturbance, but exerted no beneficial effects on gaze palsy. Then, we administered amitriptyline, bromocriptine, pergolide, 1-threo-DOPS or 5- hydroxytryptophan (5-HTP) in addition to L-dopa/carbidopa. The second patient was treated by the monotherapy of L-dopa/carbidopa, amitriptyline, 1-threo- DOPS or 5-HTP. We interposed two to three weeks between administration of each drug. In both patients, amitriptyline (75mg/day) markedly improved both gait disturbance and horizontal gaze palsy, 5-HTP (600mg/day) also improved horizontal gaze palsy, but failed to alleviate gait disturbance. The results suggest the involvement of impaired serotonergic system in ophthalmoplegia of PSP.

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ACCESSION NUMBER: 1996:475219 BIOSIS
DOCUMENT NUMBER: PREV199699204775
TITLE: Drug therapy for Parkinson's disease.
AUTHOR(S): Charles, P. David [Reprint author]; Davis, Thomas L.
CORPORATE SOURCE: 352 MCS, 2100 Pierce Ave., Nashville, TN 37212, USA
SOURCE: Southern Medical Journal, (1996) Vol. 89, No. 9,
pp. 851-856.
CODEN: SMJOAV. ISSN: 0038-4348.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Oct 1996
Last Updated on STN: 24 Oct 1996

AB Parkinson's disease (PD) is a common neurodegenerative disease characterized by tremor, rigidity, bradykinesia, and loss of postural reflexes. Although the agents available for symptomatic treatment now allow most parkinsonian patients to live a normal life-span, these patients become progressively unable to participate in social functions, perform activities of daily living, and work. Therapy for PD may be associated with many complications that contribute to these disabilities. For this reason, education is helpful for the patient newly diagnosed with PD. Over the past 6 years, three new medications (selegiline, pergolide, and controlled-release levodopa) have been approved for use in Parkinson's disease. Other agents now available for the treatment of psychiatric illness may also be helpful in selected cases of PD. With this in mind, we review the commonly prescribed drugs and outline a rational plan for treatment of parkinsonism.

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STN DUPLICATE 128

ACCESSION NUMBER: 1996:385106 BIOSIS
DOCUMENT NUMBER: PREV199699107462
TITLE: Treatment of early Parkinson's diseases: Are complicated

strategies justified?.

AUTHOR(S): Ahlskog, J. Eric
CORPORATE SOURCE: Dep. Neurology, Mayo Clinic Rochester, 200 First St. SW,
Rochester, MN 55905, USA
SOURCE: Mayo Clinic Proceedings, (1996) Vol. 71, No. 7,
pp. 659-670.
CODEN: MACPAJ. ISSN: 0025-6196.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Aug 1996
Last Updated on STN: 26 Aug 1996

AB A variety of medical treatment strategies have been proposed as a means of slowing the progression of Parkinson's disease. This includes administration of selegiline (deprenyl) therapy, early use of bromocriptine or pergolide, and delay of levodopa therapy or restriction of the dose. There is no compelling evidence supporting the use of any of these treatment strategies for this purpose. Carbidopa-levodopa remains the most potent medication for symptomatic treatment of Parkinson's disease. Although starting levodopa therapy with the controlled-release formulation is advocated, this does not appear to have any major advantages over standard carbidopa-levodopa. Further studies are needed to identify other means of halting the progression of Parkinson's disease.

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ACCESSION NUMBER: 1996251706 EMBASE
TITLE: Controversies in the treatment of Parkinson's disease.
AUTHOR: Hely, Mariese A.; Morris, John G.L. (correspondence)
CORPORATE SOURCE: Department of Neurology, Westmead Hospital, Sydney, NSW 2145, Australia.
SOURCE: Current Opinion in Neurology, (1996) Vol. 9, No. 4, pp. 308-313.
Refs: 43
ISSN: 1350-7540 CODEN: CONEEX
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Sep 1996
Last Updated on STN: 17 Sep 1996

AB Although theoretical reasons exist for believing that selegiline slows the progression of Parkinson's disease, this has not been shown in clinical trials. Selegiline improves the symptoms of Parkinson's disease, allowing the introduction of levodopa to be delayed in de-novo patients and, later, for levodopa to be used at a lower dose. It does not lessen the long-term problems of dyskinesia and fluctuations associated with levodopa therapy. The report of an increased mortality associated with selegiline therapy awaits further evaluation. Of the dopamine agonists, pergolide appears to be more potent than bromocriptine; cabergoline looks promising. The catechol-O-methyltransferase inhibitors, tolcapone and entacapone, prolong the duration of action of levodopa and also show promise. The main objective in the drug treatment of Parkinson's disease remains the optimization of the dose and frequency of levodopa administration.

L9 ANSWER 168 OF 331 MEDLINE on STN DUPLICATE 130
ACCESSION NUMBER: 2008462765 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 18638876

TITLE: An Australian multicentre open label study of pergolide as an adjunct to levodopa in Parkinson's disease.
AUTHOR: Hely M A; Morris J G; Burns R J; Lander C M; McLaughlin D B; Donnan G A
CORPORATE SOURCE: Dept of Neurology, Westmead Hospital, Sydney, NSW 2145, Australia.
SOURCE: Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia, (1996 Jul) Vol. 3, No. 3, pp. 234-8.
JOURNAL code: 9433352. ISSN: 0967-5868.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED
ENTRY DATE: Entered STN: 22 Jul 2008
Last Updated on STN: 1 Jan 2009

AB The efficacy and side effects of pergolide, a D(1) and D(2) dopamine agonist, were assessed in an open label study in 39 patients with long standing Parkinson's disease complicated by end of dose failure and/or dyskinesia. 27 patients completed 28 weeks of the study. The mean dose of pergolide was 2.26 mg/day (0.15-5.0mg/day). Levodopa was reduced by a mean of 273 mg/day (range 0-1950mg/day) from the initial mean dose of 920 mg/day (range 150-2950mg/day). Hours in which the drug was efficacious significantly increased. Dyskinesia and dystonia were significantly reduced. The scores on an abbreviated Parkinson's disease rating scale significantly improved in both the 'on' and 'off' periods. 11 patients withdrew due to early side effects but the majority of patients tolerated pergolide well. In these patients pergolide was an effective adjunct to levodopa.

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ACCESSION NUMBER: 1996:418398 BIOSIS
DOCUMENT NUMBER: PREV199699140754
TITLE: Apomorphine is a highly potent free radical scavenger in rat brain mitochondrial fraction.
AUTHOR(S): Gassen, Michael; Glinka, Yelena; Pinchasi, Bilha; Youdim, Moussa B. H. [Reprint author]
CORPORATE SOURCE: Dep. Pharmacol., Bruce Rappaport Fac. Med., Technion, PO Box 9649, Haifa 31096, Israel
SOURCE: European Journal of Pharmacology, (1996) Vol. 308, No. 2, pp. 219-225.
CODEN: EJPHAZ. ISSN: 0014-2999.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Sep 1996
Last Updated on STN: 10 Sep 1996

AB Ergoline-derived dopamine receptor agonists, like pergolide or bromocriptine, have recently attracted attention as potential neuroprotective drugs. The classical mixed type dopamine D-1 and D-2 receptor agonist apomorphine, although used clinically in the therapy of Parkinson's disease, has never been examined for any properties related to neuroprotection. In this paper, we examine the effects of 0.1-100 μ M apomorphine on ascorbate/iron-stimulated free radical processes in rat brain mitochondrial fraction. Lipid peroxidation as assayed by the thiobarbituric acid reaction can be completely inhibited by submicromolar concentrations of apomorphine (0.3 μ M with 2.5 μ M Fe-2+ and 0.6 μ M with 5.0 μ M Fe-2+), which proved to be more than twice as effective as desferrioxamine and twenty times as compared with dopamine. The inhibition of lipid peroxidation in mitochondria correlates with an increased rate of apomorphine oxidation. The formation of protein carbonyls, which is generally less sensitive to antioxidants, could be

significantly reduced by apomorphine. In the model system we employed, apomorphine was more active than dopamine, desferrioxamine, or pergolide in preventing the formation of thiobarbituric reactive substances. The time course of the reaction suggests that apomorphine acts as a radical scavenger and that its iron chelating properties may not be of major importance. Since oxidative stress has been implicated in Parkinson's disease, the role of apomorphine as a neuroprotective is worthy of examination.

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ACCESSION NUMBER: 1996:467811 BIOSIS
DOCUMENT NUMBER: PREV199699190167
TITLE: An open label trial of pergolide in Thai patients with
Parkinson's disease.
AUTHOR(S): Pongvarin, Nippon; Prayoonwivat, Naraporn; Devahasatin,
Vorapun; Viriyavejakul, Adulya
CORPORATE SOURCE: Div. Neurol., Dep. Med., Fac. Med., Siriraj Hosp., Mahidol
Univ., Bangkok 10700, Thailand
SOURCE: Journal of the Medical Association of Thailand, (
1996) Vol. 79, No. 4, pp. 205-209.
CODEN: JMTBHU. ISSN: 0125-2208.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Oct 1996
Last Updated on STN: 11 Oct 1996

AB Fifteen Thai patients with Parkinson's disease (7 females, 8 males) were enrolled in an open label trial of pergolide (a new dopamine agonist) to evaluate its safety and efficacy. Inpatients and outpatients from Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand from 1992 to 1994 were included in the study with a total duration of 18 weeks. Both de novo patients and patients who were being treated with levodopa without dopamine agonist and were obtaining a less than optimal response at both visit 1 and visit 2 were all enrolled in this study. At entry into the study, 3 patients had Hoehn and Yahr stage I, 7 patients at stage II, 3 patients at stage III, and 2 patients at stage IV. Pergolide dosage was gradually built up until an optimal dosage was achieved. The average dose of pergolide during the study was 0.94 mg/day (range 0.075 to 8 mg/day). All patients completed the study and no patients dropped out. Two patients (13.33 per cent) experienced nausea (on 0.4 mg/ day and 0.075 mg/day), two patients (13.33 per cent) experienced sleepiness (0.50 mg/day and 0.075 mg/day) and one patient (6.67 per cent) unsteadiness on walking (0.50 mg/day). There was one patient who required pergolide up to 8 mg/day which is higher than the recommended dosage (5 mg/day) but this patient experienced no adverse effects and his disabled dyskinesia was abolished. Our study demonstrated the good toleration and efficacy of pergolide treatment for Thai patients with Parkinson's disease. This new dopamine agonist stimulates both D-1 and D-2 receptors in comparison to other dopamine agonists (bromocriptine and lisuride) which stimulate only D-2 receptors.

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ACCESSION NUMBER: 1996:273896 BIOSIS
DOCUMENT NUMBER: PREV199698830025
TITLE: Enhancement of human motor cortex inhibition by the
dopamine receptor agonist pergolide: Evidence from
transcranial magnetic stimulation.
AUTHOR(S): Ziemann, Ulf [Reprint author]; Bruns, Dirk; Paulus, Walter
CORPORATE SOURCE: Dep. Clin. Neurophysiol., Univ. Goettingen,
Robert-Koch-Str. 40, D-37075 Goettingen, Germany

SOURCE: Neuroscience Letters, (1996) Vol. 208, No. 3, pp. 187-190.

CODEN: NELED5. ISSN: 0304-3940.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 10 Jun 1996

Last Updated on STN: 10 Jun 1996

AB Focal transcranial magnetic stimulation was used to evaluate the effect a single oral dose (0.125 mg) of the dopamine agonist pergolide on the excitability of the motor cortex in five healthy subjects. Resting and active motor thresholds of the abductor digiti minimi muscle were unaffected. The mean duration of the cortical silent period was significantly lengthened by up to 22 ms. The cortico-cortical inhibition as studied by a paired conditioning-test stimulation (interstimulus intervals of 1-5 ms) was enhanced significantly while the cortico-cortical facilitation at longer intervals (6-15 ms) showed only an insignificant trend towards less facilitation. All effects peaked at 3 h after drug intake and were reversible after 24 h. Peripheral motor excitability as tested by the duration of the peripheral silent period and the size of the maximum M wave remained unchanged. The present data support the view that pergolide is capable of enhancing motor cortex inhibition which is known to be deficient in idiopathic Parkinson's disease.

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ACCESSION NUMBER: 1996057043 EMBASE

TITLE: The levodopa dose-sparing capacity of pergolide compared with that of bromocriptine in an open-label, crossover study.

AUTHOR: Boas, J. (correspondence)

CORPORATE SOURCE: University Department of Neurology, Glostrup Hospital, 2600 Glostrup, Denmark.

AUTHOR: Worm-Petersen, J.

CORPORATE SOURCE: University Department of Neurology, Gentofte Hospital, Gentofte, Denmark.

AUTHOR: Dupont, E.

CORPORATE SOURCE: University Department of Neurology, Arhus Hospital, Arhus, Denmark.

AUTHOR: Mikkelsen, B.

CORPORATE SOURCE: Department of Neurology, Hjorring Hospital, Hjorring, Denmark.

AUTHOR: Wermuth, L.

CORPORATE SOURCE: University Department of Neurology, Odense Hospital, Odense, Denmark.

SOURCE: European Journal of Neurology, (1996) Vol. 3, No. 1, pp. 44-49.

Refs: 23

ISSN: 1351-5101 CODEN: EJNEFL

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 037 Drug Literature Index

008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 25 Mar 1996

Last Updated on STN: 25 Mar 1996

AB The levodopa dose-sparing capacity of pergolide and bromocriptine, along with the maximum ability to improve activity of daily living and motor scores, were compared in 33 patients with idiopathic Parkinson's disease (Hoehn-Yahr stage 2-4) in a 24-week, open-label, crossover study. Patients received one dopamine agonist for 12 weeks and then were crossed over to the other for 12 weeks (8 weeks,

titration; 4 weeks, steady state in each period). The maximum doses allowed were pergolide 5 mg/day and bromocriptine 50 mg/day. As patients' clinical response to a dopamine agonist increased, the levodopa dose was decreased. Twenty-seven patients completed the study. No serious adverse events or clinically significant changes in vital signs or laboratory tests were observed. The mean doses of bromocriptine and pergolide at the end of titration were 21.7 ± 5.6 mg (bromocriptine data for the two groups combined) and 3.6 ± 1.1 mg (pergolide data for the two groups combined), respectively. The mean levodopa dose was reduced 8.3% with bromocriptine as the first agent and increased 28.0% with bromocriptine as the second agent. The mean levodopa dose was reduced 31.4% with pergolide as the first agent and 15.5% with pergolide as the second agent. Levodopa could not be discontinued in any of the patients. Statistically significant levodopa dose-sparing capacity and considerable clinical benefit were achieved with both agonists; however, the results were more favorable with pergolide.

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ACCESSION NUMBER: 1996:514470 BIOSIS
DOCUMENT NUMBER: PREV199699236826
TITLE: Inhibition of dopamine neuron firing by pramipexole, a dopamine D-3 receptor-preferring agonist: Comparison of other dopamine receptor agonists.
AUTHOR(S): Piercey, Montford F. [Reprint author]; Hoffmann, William E.; Smith, Martin W.; Hyslop, Deborah K.
CORPORATE SOURCE: CNS Res. 7251-209-419, Pharm. Upjohn Inc., 301 Henrietta St., Kalamazoo, MI 49001, USA
SOURCE: European Journal of Pharmacology, (1996) Vol. 312, No. 1, pp. 35-44.
CODEN: EJPHAZ. ISSN: 0014-2999.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Nov 1996
Last Updated on STN: 14 Nov 1996

AB Pramipexole, an amino-benzothiazole ((S)-4,5,6,7-tetrahydro-N-6-propyl-2,6-benzothiazolediamine dihydrochloride monohydrate) direct-acting dopamine receptor agonist effective in treating Parkinson's disease. bound selectively and with high affinity to dopamine D2-like receptors, with highest affinity at dopamine D-3 receptors. Ergot dopamine receptor agonists (bromocriptine, lisuride, pergolide) bound to both dopamine and non-dopamine receptors. Although all agonists depressed dopamine neuron firing, only pramipexole and quinpirole completely silenced firing when administered in slowly-accumulating doses. High-dose pergolide, but not other ergots, completely suppressed firing when given by a prompt bolus i.v. injection, suggesting efficacy limitations may have involved receptor desensitization for pergolide, but not for bromocriptine and lisuride. We conclude that pramipexole differs from ergot dopamine receptor agonists currently used in the treatment of Parkinson's disease by virtue of its selectivity for dopamine receptors, its preferential affinity for the dopamine D-3 receptor subtype, and its greater efficacy for stimulating dopamine receptors, as indicated in these electrophysiology assays.

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ACCESSION NUMBER: 1996:84011 BIOSIS
DOCUMENT NUMBER: PREV199698656146
TITLE: Analysis of mortality in pergolide-treated patients with Parkinson's disease.

AUTHOR(S): Sayler, Mary E. [Reprint author]; Street, Jamie S.;
Bosomworth, Janet C.; Potvin, Janet H.; Kotsanos, James G.
CORPORATE SOURCE: Eli Lilly Co., Lilly Corp. Cent., Mail Drop Code 2233,
Indianapolis, IN 46285, USA
SOURCE: Neuroepidemiology, (1996) Vol. 15, No. 1, pp.
26-32.
ISSN: 0251-5350.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Feb 1996
Last Updated on STN: 28 Feb 1996

AB Parkinson's disease, because of its progressive degenerative nature, is associated with increased disability and mortality compared with mortality in the general population. We examined mortality data from three clinical trials involving 1,330 patients with Parkinson's disease treated with pergolide as an adjunct to levodopa or levodopa/carbidopa therapy. The ratio of observed deaths to expected deaths in the general population of the same age, gender, race distribution, and period of observation was 2.3 for the 3 studies combined. The ratio is lower than that in Parkinson's disease patients treated prior to the introduction of levodopa, consistent with ratios with levodopa and levodopa combination therapy. The ratio is slightly higher than in Parkinson's disease patients treated with levodopa and levodopa combination therapy, which may be attributable to differing patient characteristics in the populations studied.

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STN DUPLICATE 137

ACCESSION NUMBER: 1996:475363 BIOSIS
DOCUMENT NUMBER: PREV199699204919
TITLE: Effect of U-91356A, a potential anti-Parkinsonian drug, on striatal acetylcholine concentration.
AUTHOR(S): Sethy, Vimala H. [Reprint author]; Ellerbrock, Brenda R.; Nichols, Nan F.
CORPORATE SOURCE: CNS Res. 7251-209-508, Pharmacia and Upjohn Inc., 301 Henrietta St., Kalamazoo, MI 49001, USA
SOURCE: Drug Development Research, (1996) Vol. 38, No. 1, pp. 24-30.
CODEN: DDREDK. ISSN: 0272-4391.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Oct 1996
Last Updated on STN: 24 Oct 1996

AB Antiparkinsonian drugs are dopamine agonists and they have been reported to increase striatal acetylcholine (ACh) concentrations. U-91356A is a D-2 selective dopamine agonist. Therefore, it was investigated for its effect on rat striatal ACh concentration, and the results were compared with those obtained with pergolide and quinpirole under similar conditions. U-91356A was as potent as pergolide and less potent than quinpirole in increasing striatal ACh in nonreserpinized rats. The intrinsic activity of U-91356A was significantly ($P < 0.03$) greater than pergolide in non-reserpinized rats. In reserpinized rats, the potency of investigated dopamine agonists was similar for elevating ACh levels, and intrinsic activity of U-91356A ($P < 0.01$) was higher as compared to that obtained with quinpirole or pergolide. In the unilateral substantia nigra lesioned animals, the intrinsic activity of U-91356A for increasing striatal ACh was significantly ($P < 0.01$) higher in the denervated, as compared to innervated, striatum. The supersensitive response of quinpirole and pergolide for increasing striatal ACh was also observed on the lesioned as compared to intact side. Haloperidol significantly ($P < 0.01$) blocked U-91356A-induced elevation in striatal

ACh in non-reserpinized rats. Based on these results, U-91356A appears to be a potent agonist of striatal post-synaptic D-2 dopamine receptors and is expected to be an effective anti-parkinsonian drug.

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ACCESSION NUMBER: 1996189789 EMBASE
TITLE: Dopamine agonists in the clinical management of Parkinson's disease: Symptomatic or neuroprotective treatment?.
AUTHOR: Bravi, D. (correspondence); Megas, L.F.
CORPORATE SOURCE: Department of Neuroscience, Eli Lilly Italia, Italy.
AUTHOR: Nohria, V.
CORPORATE SOURCE: Regional Medical Centre, Eli Lilly and Company, United Kingdom.
AUTHOR: Bravi, D. (correspondence)
CORPORATE SOURCE: Eli Lilly Italia SpA, via Gramsci 731-733, Sesto Fiorentino, I-50019 Florence, Italy.
SOURCE: European Journal of Neurology, (1996) Vol. 3, No. SUPPL. 1, pp. 13-18.
Refs: 37
ISSN: 1351-5101 CODEN: EJNEFL
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 22 Jul 1996
Last Updated on STN: 22 Jul 1996

AB There is no doubt that levodopa treatment remains one of the major advances in the clinical management of parkinsonian patients. However, the efficacy of levodopa decreases after several years and motor complications appear. Dopamine agonists stimulate directly the spared postsynaptic dopaminergic system of the striatum, therefore bypassing presynaptic dopamine metabolism. DAs including pergolide, bromocriptine, lisuride, and apomorphine exert a clear symptomatic, antiparkinsonian effect. Furthermore, long term treatment with DAs does not seem to be associated with motor fluctuations. Recently, preclinical data have shown that DAs, notably pergolide, have protective effects on nigral neurons. This paper discusses issues associated with levodopa toxicity and the complications of its treatment as well as the question of whether agonists, in addition to their symptomatic effect, also have a protective action in Parkinson's disease.

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ACCESSION NUMBER: 1996189788 EMBASE
TITLE: The levodopa dose-sparing capacity of pergolide compared with that of bromocriptine.
AUTHOR: Dupont, E. (correspondence)
CORPORATE SOURCE: Department of Neurology, Arhus University Hospital, 8000 Arhus C, Denmark.
AUTHOR: Boas, J.
CORPORATE SOURCE: University Department of Neurology, Glostrup Hospital, Glostrup, Denmark.
AUTHOR: Mikkelsen, B.
CORPORATE SOURCE: Department of Neurology, Hjorring Hospital, Hjorring, Denmark.
AUTHOR: Wermuth, L.
CORPORATE SOURCE: Department of Neurology, Odense University Hospital,

Odnese, Denmark.
AUTHOR: Worm-Petersen, J.
CORPORATE SOURCE: University Department of Neurology, Gentofte Hospital,
Gentofte, Denmark.
SOURCE: European Journal of Neurology, (1996) Vol. 3, No.
SUPPL. 1, pp. 9-12.
Refs: 21
ISSN: 1351-5101 CODEN: EJNEFL
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 22 Jul 1996
Last Updated on STN: 22 Jul 1996

AB This multicentre, open-label, crossover study compared the effects of pergolide and bromocriptine in combination with levodopa in the treatment of 33 patients with idiopathic Parkinson's disease. The aim of the study was to compare clinical efficacy and levodopa-dose-sparing effects of the two drugs. Pergolide, given as either the first or second treatment, reduced the required dose of levodopa. On the other hand, bromocriptine given as the first therapy reduced this dose, whereas when it was used following pergolide treatment, the required dose of levodopa increased. Overall, pergolide had significantly greater levodopa-dose-sparing effects than bromocriptine. Similar results were obtained for clinical efficacy. Pergolide used as either the first or second treatment produced a reduction in motor symptoms, whereas bromocriptine used first produced a reduction, but as a second treatment produced an increase in motor symptoms. Overall, pergolide produced greater clinical benefits than bromocriptine. Both treatments were equally well tolerated, The main side effect was nausea, which was reported by four patients receiving each treatment. No serious adverse events were reported. It is concluded that both pergolide and bromocriptine are useful adjuncts to levodopa therapy. Furthermore, pergolide appeared to be superior to bromocriptine.

L9 ANSWER 178 OF 331 MEDLINE on STN DUPLICATE 140
ACCESSION NUMBER: 1996019379 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7487655
TITLE: Treatment of Parkinson's disease.
AUTHOR: Eadie M J
CORPORATE SOURCE: Department of Medicine, University of Queensland.
SOURCE: Australian family physician, (1995 Sep) Vol. 24,
No. 9, pp. 1685-7, 1690-2.
Journal code: 0326701. ISSN: 0300-8495.
PUB. COUNTRY: Australia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 24 Jan 1996
Last Updated on STN: 24 Jan 1996
Entered Medline: 13 Dec 1995

AB Early stage Parkinson's disease may be better left untreated if it does not limit motor function. Once limitation of function is present levodopa-dopa decarboxylase inhibitor combinations are the most effective therapy, although amantadine may be satisfactory for a time in milder cases. The optimal independent roles of the ergot derivatives bromocriptine and pergolide, and the MAOb inhibitor selegiline,

are not yet generally agreed although they are accepted as useful in supplementing the effects of levodopa. With prolonged levodopa use various late-stage treatment problems may appear. The pathogenesis of these is poorly understood and no completely satisfactory ways of managing them are available.

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ACCESSION NUMBER: 1996:39785 BIOSIS
DOCUMENT NUMBER: PREV199698611920
TITLE: Dopamine agonists used in the treatment of Parkinson's disease and their selectivity for the D-1, D-2, and D-3 dopamine receptors in human striatum.
AUTHOR(S): De Keyser, Jacques [Reprint author]; De Backer, Jean-Paul; Wilczak, Nadine; Herroelen, Luc
CORPORATE SOURCE: Janssen Res. Foundation, Turnhoutseweg 30, B 2340 Beerse, Belgium
SOURCE: Progress in Neuro-Psychopharmacology and Biological Psychiatry, (1995) Vol. 19, No. 7, pp. 1147-1154.
CODEN: PNPPD7. ISSN: 0278-5846.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jan 1996
Last Updated on STN: 27 Jan 1996

AB It has been suggested that an ideal antiparkinsonian treatment requires stimulation of both D-1 and D-2 dopamine receptors. Bromocriptine and lisuride are regarded as pure D-2 receptor agonists, whereas pergolide and apomorphine are thought to stimulate both D-1 and D-2 receptors. The aim of this study was to compare the affinities of bromocriptine, lisuride, pergolide, and apomorphine for the D-1, D-2, and D-3 receptors in postmortem human striatum. The dissociation constants (K_i values) of the dopamine agonists were determined from competition binding experiments with selective radioligands. The K_i values of the orally administered agonists - bromocriptine, pergolide, and lisuride - for the D-2 receptors were proportional to their optimal doses against parkinsonism. $K_i(D-1)/K_i(D-2)$ ratios were 23 for lisuride, 67 for pergolide, 60 for bromocriptine, and 2.6 for apomorphine. $K_i(D-3)/K_i(D-2)$ ratios were 0.4 for lisuride, 1 for pergolide, 5.4 for bromocriptine, and 21 for apomorphine. The present results support the hypothesis that the antiparkinsonian effect of dopamine agonists is mediated primarily by D-2 receptors. Apomorphine is a mixed D-1/D-2 agonist, but pergolide has no more D-1 agonist properties than bromocriptine and lisuride. The role of the D-3 receptors is unknown, but their activation might either be associated with the generation of psychiatric side-effects or dyskinesias, or alternatively add to antiparkinsonian activity.

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ACCESSION NUMBER: 1996:164588 BIOSIS
DOCUMENT NUMBER: PREV199698736723
TITLE: Retroperitoneal fibrosis in patients with Parkinson's disease treated with L-dopa analogues.
AUTHOR(S): Sanchez-Chapado, Manuel [Reprint author]; Angulo Cuesta, Javier; Guil Cid, Manuel; Javier Jimenez, Francisco; Lopez Alvarez, Joaquin
CORPORATE SOURCE: Serv. Urol., Hosp. Principe Asturias, Carretera Alcala-Meco s/n, 28800 Alcala de Henares, Madrid, Spain
SOURCE: Archivos Espanoles de Urologia, (1995) Vol. 48, No. 10, pp. 979-983.
CODEN: AEURAB. ISSN: 0004-0614.

DOCUMENT TYPE: Article
LANGUAGE: Spanish
ENTRY DATE: Entered STN: 11 Apr 1996
Last Updated on STN: 10 Jun 1997

AB OBJECTIVES: The present study describes two patients with retroperitoneal fibrosis following prolonged use of bromocriptine and pergolide for Parkinson's disease. Both patients also presented severe atheromatosis. METHODS: Similar cases reported in the literature are reviewed and the possible relationship between the use of the ergotamine derivate and severe atheromatosis is discussed. RESULTS: Both patients, a 67-year-old male and a 62-year-old female, improved after discontinuing bromocriptine, despite severe damage of renal function. CONCLUSIONS: Retroperitoneal fibrosis may develop in patients with bilateral ureteral obstruction, especially those who have received drugs that have been reported to cause the foregoing condition.

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ACCESSION NUMBER: 1996046594 EMBASE
TITLE: Chronic L-DOPA administration induces dyskinesias in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-treated common marmoset (*Callithrix jacchus*).
AUTHOR: Pearce, R.K.B.; Jackson, M.; Smith, L.; Jenner, P., Prof. (correspondence); Marsden, C.D.
CORPORATE SOURCE: Pharmacology Group, Biomedical Sciences Division, King's College, Manresa Road, London SW3 6LX, United Kingdom.
SOURCE: Movement Disorders, (1995) Vol. 10, No. 6, pp. 731-740.
ISSN: 0885-3185 CODEN: MOVDEA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Feb 1996
Last Updated on STN: 20 Feb 1996

AB Dyskinesias occur in the majority of patients with Parkinson's disease chronically treated with L-DOPA and also occur in several nonhuman primate species after 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and L-DOPA treatment. The common marmoset (*Callithrix jacchus*) shows parkinsonian motor deficits after MPTP administration, and we now report dyskinesias occurring in this species during chronic L-DOPA exposure. Marmosets rendered chronically parkinsonian after MPTP administration were treated orally with L-DOPA plus carbidopa for 3 weeks. After several days the animals began to display chorea, choreoathetosis, and dystonia. The severity of dyskinesias varied between the animals, with the most severely parkinsonian animals displaying the most dyskinetic movements. Each animal showed an idiosyncratic pattern of dyskinesias, which was highly reproducible. These L-DOPA-primed animals also received other D(2), D(1), and mixed D(1)/D(2) agonist drugs. Quinpirole, bromocriptine, pergolide, apomorphine, and A-77636 all produced dyskinesias that were identical in character to those seen after L-DOPA administration, but the D(1) agonist A-77636 gradually abolished dyskinesias while preserving its antiparkinsonian activity. The MPTP-treated marmoset provides a useful model in which to study dyskinesias in Parkinson's disease and to examine new therapeutic strategies aimed at alleviating this common side effect of chronic dopamine replacement therapy.

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DUPLICATE 144

ACCESSION NUMBER: 1995286250 EMBASE
TITLE: A 'combined' levodopa test as a useful method for
evaluating the efficacy of dopamine agonists: Application
to pergolide and bromocriptine.
AUTHOR: Bonnet, A.M., Dr. (correspondence); Serre, I.; Marconi, R.;
Agid, Y.; Dubois, B.
CORPORATE SOURCE: Federation de Neurologie, Hopital de la Salpetriere, 47 Bd
de l'Hopital, 75013 Paris, France.
SOURCE: Movement Disorders, (1995) Vol. 10, No. 5, pp.
668-671.
ISSN: 0885-3185 CODEN: MOVDEA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 10 Oct 1995
Last Updated on STN: 10 Oct 1995

AB The efficacy of pergolide as adjunct to levodopa therapy was
compared to that of bromocriptine in 12 parkinsonian patients
with fluctuating motor disability and levodopa-induced dyskinesias (mean
age of onset, 50.6 ± 8 years; Hoehn and Yahr stage between II and IV;
mean basal UPDRS motor score, 30.6 ± 8.6), in a double-blind crossover
study. After an 8-day habituation to each agonist, an acute challenge of
a supraliminal dose of levodopa ('levodopa test') was performed in
association with either 1 mg pergolide or 10 mg bromocriptine.
The delay to onset and the duration of therapeutic benefit, the percentage
improvement in motor disability, and the severity of onset and peak-dose
dyskinesias were evaluated. Both agonists significantly increased the
duration of therapeutic benefit, but pergolide more so than
bromocriptine ($p = 0.02$). Pergolide also tended to reduce the
severity of dyskinesias and was globally perceived by the patients to be
more efficacious than bromocriptine on parkinsonian symptoms and
fluctuations. This study illustrated the usefulness of the 'levodopa
test' in evaluating, objectively, the effects of dopamine agonists.

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DUPLICATE 145

ACCESSION NUMBER: 1995167273 EMBASE
TITLE: 'Off' painful dystonia in Parkinson's disease treated with
botulinum toxin.
AUTHOR: Pacchetti, C., Dr. (correspondence); Albani, G.;
Martignoni, E.; Godi, L.; Alfonsi, E.; Nappi, G.
CORPORATE SOURCE: Parkinson's Disease Centre, IRCSS 'C Mondino', via Palestro
3, 27100 Pavia, Italy.
SOURCE: Movement Disorders, (1995) Vol. 10, No. 3, pp.
333-336.
ISSN: 0885-3185 CODEN: MOVDEA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Jun 1995
Last Updated on STN: 19 Jun 1995

AB The 'off' painful dystonia (OPD), usually concerning the feet, is a type
of abnormal involuntary movement, induced by the chronic use of levodopa.

It is mostly observed in the advanced stage of Parkinson's disease (PD), particularly in the early morning, in the evening, and late at night. Indeed, some patients have experienced OPD also during 'on' periods when dystonic posture of the foot alternates with dyskinesia. The pain probably is due to sustained muscle contraction, which causes prolonged muscle spasm, as in primary dystonia or torticollis. Dopaminergic drugs like bromocriptine, pergolide, and especially apomorphine (s.c., infusions, or bolus), can dramatically improve the OPD. Anticholinergics baclofen and lithium are also used in the management of OPD with some benefit. On the other hand, clinical experience shows that in many cases, these therapeutic procedures are not always enough to produce the expected results. Thirty PD patients (22 men and eight women) with OPD of the foot were treated with botulinum toxin (Botox, Btx) using electromyograms to guide injections. Dystonia was evaluated using a quantitative rating scale. The selection of the muscles for Btx treatment was carried out on the basis of foot posture. We injected Btx into tibialis posterior, tibialis anterior, gastrocnemius, flexor digitorum longus, and extensores hallucis longus with a median dose 40 IU for each muscle, distributed in two sites. In all patients, the pain improved within 10 days, whereas in 21 patients, the pain disappeared completely for 4 months (range, 3-7 months); a concomitant improvement in intensity of the dystonic spasm was also observed. No side effects were reported. Seven patients with associated 'on' foot dystonia described an improvement of foot posture on walking. In conclusion, in this uncontrolled study, the use of Btx in OPD seemed a promising tool to improve pain linked to foot dystonia; however, because of the well-known underlying dopaminergic defect in OPD, the Btx therapy should be considered only if the dopaminergic treatment established for the management of OPD has failed.

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ACCESSION NUMBER: 1996033059 EMBASE
 TITLE: Experience of pergolide in the treatment of Chinese parkinsonian patients with dose-related fluctuations.
 AUTHOR: Shan, D.-E., Dr. (correspondence); Yeh, S.-I.
 CORPORATE SOURCE: Neurological Institute, Veterans General Hospital, Taipei, Taiwan, Province of China.
 SOURCE: Chinese Medical Journal (Taipei), (1995) Vol. 56, No. 5, pp. 312-318.
 ISSN: 0578-1337 CODEN: CIHCDM
 COUNTRY: Taiwan, Province of China
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 037 Drug Literature Index
 038 Adverse Reactions Titles
 008 Neurology and Neurosurgery
 LANGUAGE: English
 SUMMARY LANGUAGE: English; Chinese
 ENTRY DATE: Entered STN: 20 Feb 1996
 Last Updated on STN: 20 Feb 1996

AB Background. To improve dose-related fluctuations in patients with Parkinson's disease, the efficacy of pergolide, a long-acting dopamine receptor agonist, was determined. Methods. Using a stringent diagnostic criterion for Parkinson's disease, 20 patients were selected for a short-term open-label trial, and were divided into three groups based on the accuracy of clinical diagnosis. Results. Nineteen patients completed the study. The mean dosage of pergolide was 2.89 mg per day. The total motor score improved by 34.1% during the 'on' period and by 34.8% during the 'off' period. ($p < 0.001$). The recorded daily off time decreased from 40.3% to 11.5% ($p < 0.001$). There was no statistically significant difference in the magnitude of response among different groups of patients; however, patients with shorter duration of illness also received significantly

lower dosage of pergolide. Hallucination, worsening of peak-dose dyskinesia, and lowering of blood pressure were major adverse effects. Pergolide could not prevent the occurrence of neuroleptic malignant syndrome in one patient. Conclusions. Pergolide is very effective for moderate to advanced Parkinson's disease.

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ACCESSION NUMBER: 1995167270 EMBASE
TITLE: Antiparkinsonian therapies and brain mitochondrial complex I activity.
AUTHOR: Przedborski, S., Dr. (correspondence); Jackson-Lewis, V.; Fahn, S.
CORPORATE SOURCE: Department of Neurology, College of Physicians and Surgeons, Columbia University, 650 West 168th Street, New York, NY 10032, United States.
SOURCE: Movement Disorders, (1995) Vol. 10, No. 3, pp. 312-317.
ISSN: 0885-3185 CODEN: MOVDEA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical and Experimental Biochemistry
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Jun 1995
Last Updated on STN: 19 Jun 1995

AB Alterations in complex I activity, one of the enzymatic units of the mitochondrial respiratory chain, have been demonstrated in different tissues from patients with Parkinson's disease (PD). Subsequently, we showed that the chronic administration of levodopa can cause alterations in mitochondrial respiratory chain activity in rats, which suggests that the observed deficit in complex I activity in PD might be, at least in part, related to chronic levodopa therapy. Our study assessed the in vitro effects of different antiparkinsonian agents on complex I activity in rat brain. As previously reported, both levodopa and dopamine inhibit complex I activity in a dose-dependent manner. In contrast, the two major metabolites of dopamine, homovanillic acid and 3,4-dihydroxyphenylacetic acid as well as 3-O-methyl-dopa, had little or no effect on complex I activities. Bromocriptine, pergolide, trihexyphenidyl, molindone, and clozapine were all without significant inhibitory effects on mitochondrial function. Although vitamin C and deprenyl did not alter complex I activity, they did prevent the inhibitory effect of both levodopa and dopamine on complex I activity. This work indicates that among the different and usual antiparkinsonian agents, only levodopa and dopamine induced reductions in complex I activity. It also indicates that vitamin C and deprenyl are both effective in preventing the levodopa-induced complex I inhibition. This latter finding provides further support to the use of antioxidants and monoamine oxidase inhibitors as therapeutic strategies in attempts to slow the progression of PD.

L9 ANSWER 186 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 148

ACCESSION NUMBER: 1995:323244 BIOSIS
DOCUMENT NUMBER: PREV199598337544
TITLE: Retroperitoneal fibrosis in a patient with Parkinson's disease treated with pergolide.
AUTHOR(S): Jimenez-Jimenez, Felix Javier [Reprint author]; Lopez-Alvarez, Joaquin; Sanchez-Chapado, Manuel; Montero,

Eduardo; Miquel, Joaquin; Sierra, Adela; Gutierrez, Fernando
CORPORATE SOURCE: C/Corregidor Jose de Pasamonte 24, 3D, E-28030 Madrid, Spain
SOURCE: Clinical Neuropharmacology, (1995) Vol. 18, No. 3, pp. 277-279.
CODEN: CLNEDB. ISSN: 0362-5664.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jul 1995
Last Updated on STN: 30 Jul 1995

AB We describe a 68-year-old patient with Parkinson's disease who developed retroperitoneal fibrosis during pergolide treatment. Because pergolide is an ergot derivative, it could be related to the development of this complication.

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ACCESSION NUMBER: 1995:397785 BIOSIS
DOCUMENT NUMBER: PREV199598412085
TITLE: Protective Effects of Pergolide on Dopamine Levels in the 6-Hydroxydopamine-Lesioned Mouse Brain.
AUTHOR(S): Asanuma, M. [Reprint author]; Ogawa, N.; Nishibayashi, S.; Kawai, M.; Kondo, Y.; Iwata, E.
CORPORATE SOURCE: Dep. Neurosci., Inst. Mol. Cell. Med., Okayama Univ. Med. Sch., 2-5-1 Shikatacho, Okayama, Japan
SOURCE: Archives Internationales de Pharmacodynamie et de Therapie, (1995) Vol. 329, No. 2, pp. 221-230.
CODEN: AIPTAK. ISSN: 0003-9780.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Sep 1995
Last Updated on STN: 10 Oct 1995

AB Pergolide, along with bromocriptine and lisuride, is one of the most active dopamine receptor agonists. To determine whether or not pergolide protects against dopaminergic neuronal damage, via its activity on monoamine metabolism, we studied the effects of pergolide pretreatment on changes in monoamines and their metabolites in the mouse striatum after intracerebroventricular injection of 6-hydroxydopamine with pretreatment of desipramine. After intracerebroventricular administration of 6-hydroxydopamine (40 μ -g) in mice, the levels of dopamine and its metabolites (DOPAC, HVA) in the striatum rapidly decreased to 49%, 29% and 68%, respectively, of the naive controls at week 1 but then gradually recovered to control levels at weeks 2 and 4. Repeated pretreatment with pergolide (0.5 mg/kg, i.p.) for 7 days before administration of 6-hydroxydopamine, almost completely protected against reduction in striatal dopamine and its metabolites 1 week after injection of 6-hydroxydopamine. Therefore, pergolide could normalize the decreased dopamine synthesis or storage, and has a neuroprotective effect against dopaminergic dysfunction induced by the neurotoxin, 6-hydroxydopamine. Although we found that pergolide did not show radical scavenging activity in an in vitro system that generated hydroxyl radicals, it has been reported in vivo that pergolide treatment may induce Cu/Zn superoxide dismutase in the rat striatum. Considering these findings, pergolide may well be protective to dopaminergic neurons, largely because of its effects on presynaptic autoreceptors and on its induction of Cu/Zn superoxide dismutase. Further research on the neuroprotective effects of pergolide in Parkinson disease models, by injection of 6-hydroxydopamine, is needed to clarify its mechanism of action on dopaminergic indices.

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STN DUPLICATE 150

ACCESSION NUMBER: 1996:128912 BIOSIS
DOCUMENT NUMBER: PREV199698701047
TITLE: Second generation of dopamine agonists: Pros and cons.
AUTHOR(S): Rabey, J. M.
CORPORATE SOURCE: Dep. Neurol., Asaf Harofe Hosp., Zrifin 70300, Israel
SOURCE: Journal of Neural Transmission Supplement, (1995)
Vol. 45, No. 0, pp. 213-224.
CODEN: JNTSD4. ISSN: 0303-6995.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Mar 1996
Last Updated on STN: 27 Mar 1996

AB Dopamine agonists (DAGs) were first used in patients with moderate or advanced Parkinson's disease (PD). At that time, it was thought that DAGs could replace levodopa (LD) with fewer side effects. However, it soon became clear that while they could not replace LD, they did allow reduction of the dose of LD and diminished its side effects. Since the use of DAGs reduces response fluctuations as well as dyskinesias, there is a tendency to introduce them in the first stages of the disease, trying to delay motor fluctuations. While many DAGs have been developed, only four have been marketed and are used extensively for the treatment of Parkinson's disease: apomorphine, bromocriptine, lisuride and pergolide. In the present chapter, following a review of the "old" DAGs, the experience with three new promising DAGs is reported: cabergoline, ropinirole and pramipexole.

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ACCESSION NUMBER: 1995:367615 BIOSIS
DOCUMENT NUMBER: PREV199598381915
TITLE: Dopamine agonists in the treatment of Parkinson's disease.
AUTHOR(S): Pahwa, Rajesh [Reprint author]; Koller, William C.
CORPORATE SOURCE: Dep. Neurology, Univ. Kansas Med. Cent., 3901 Rainbow
Blvd., Kansas City, KS 66160, USA
SOURCE: Cleveland Clinic Journal of Medicine, (1995) Vol.
62, No. 4, pp. 212-217.
ISSN: 0891-1150.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Aug 1995
Last Updated on STN: 30 Aug 1995

AB The dopamine agonists bromocriptine and pergolide are useful adjuvants to levodopa in treating Parkinson's disease. Used this way, they can produce clinical improvement and can often permit lowering of the levodopa dosage. Bromocriptine or pergolide can be used as initial monotherapy in Parkinson's disease. When used as an adjuvant to levodopa therapy, these drugs can result in clinical improvement and a decreased levodopa requirement. To avoid side effects, the starting dosage should be low (1.25 mg per day of bromocriptine or 0.05 mg of pergolide) and should be increased slowly. The standard daily dose of bromocriptine ranges from 7.5 to 60 mg, and of pergolide, from 0.75 to 4 mg. Combination therapy with low dosages of levodopa and a dopamine agonist may also decrease the incidence of side effects of both agents.

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ACCESSION NUMBER: 1996:128911 BIOSIS

DOCUMENT NUMBER: PREV199698701046
TITLE: Pergolide mesylate in Parkinson's disease treatment.
AUTHOR(S): Pezzoli, G. [Reprint author]; Canesi, M.; Pesenti, A.;
Mariani, C. B.
CORPORATE SOURCE: Ospedale Maggiore Policlin., Pad. Ponti, Via F. Sforza 35,
I-20122 Milan, Italy
SOURCE: Journal of Neural Transmission Supplement, (1995)
Vol. 45, No. 0, pp. 203-212.
CODEN: JNTSD4. ISSN: 0303-6995.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Mar 1996
Last Updated on STN: 27 Mar 1996

AB In the past 15 years, clinical data of over 1,500 patients treated with pergolide mesylate have been published. Pergolide is a dopamine agonist with a potent stimulating effect on D2 and also on D1 receptors. This pharmacodynamic characteristic seems the most effective in increasing the motility in Parkinson's disease. Pergolide has been used almost exclusively as an adjunct to levodopa treatment. Its positive effects seems to be related to its long plasma half life, about 27 hours, and 5-6 hours of clinical activity; it has shown to be effective on all parkinsonian symptoms except for the reduction of postural reflexes, it reduces off periods and, compared to bromocriptine, it considerably improves the activities of daily living. Adverse reactions are, for the most part, mild and reversible, they mostly include nausea and gastroenteric disturbances.

L9 ANSWER 191 OF 331 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation
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ACCESSION NUMBER: 1995:831685 SCISEARCH
THE GENUINE ARTICLE: TG955
TITLE: PERGOLIDE IN THE TREATMENT OF ADVANCED PARKINSONS-DISEASE
AUTHOR: MECO G (Reprint); ALESSANDI A; FABBRINI G; ZUCHEGNA P;
PRATESI L; FABRIZIO E; VANACORE N; BONIFATI V
CORPORATE SOURCE: UNIV ROMA LA SAPIENZA, DIPARTIMENTO SCI NEUROL, I-00185
ROME, ITALY
COUNTRY OF AUTHOR: ITALY
SOURCE: GIORNALE DI NEUROPSICOFARMACOLOGIA, (SEP-OCT 1995***)
Vol. 17, No. 5, pp. 129-133.
ISSN: 0391-9048.
PUBLISHER: CIC-EDIZIONI INTERNAZIONALI SRL, VIA L SPALLANZANI,
11-00161 ROMA, ITALY.
DOCUMENT TYPE: Article; Journal
LANGUAGE: French
REFERENCE COUNT: 20
ENTRY DATE: Entered STN: 1995
Last Updated on STN: 1995
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The treatment of motor fluctuations in ***Parkinsonian patients is usually based on the use of slow release oral formulations of levodopa, or on the adjunct of orally or parenterally administered dopamine agonists. The beneficial effects of dopamine agonists in improving clinical fluctuations partially related relate on their relatively long plasma half-life and even longer behavioural effects. Dopamine agonists can also allow a different stimulation of dopamine receptor subtypes compared to levodopa.
Pergolide is a potent dopamine agonist (D1, D2, and D3 receptors), which is able to reduce the dosage of co-administered levodopa with concomitant improvement in disability.
The objective of this study was to evaluate whether the addition of Pergolide to levodopa therapy could decrease motor fluctuations

without concomitant increase in dyskinesias, eventually with a reduction in the total daily dose of levodopa.

Pergolide was added in an open fashion to previously (at least 1 month) stabilized doses of levodopa + IDD in 25 patients, all with fluctuations in motor performances.

In our patients the addition of Pergolide (mean dose = 1.63 +/- 1.43 mg/day) to levodopa therapy, allowed to reduce disability and also levodopa daily doses (mean reduction = 14.3%) without a concomitant increase in dyskinesias and with not significant psychiatric side effects.

L9 ANSWER 192 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1995:924732 CAPLUS

TITLE: Genesis and development of a one-pot synthesis of pergolide.

AUTHOR(S): Misner, Jerry W.

CORPORATE SOURCE: Division Eli Lilly and Company, Lilly Research Laboratories, Indianapolis, IN, 46285-4813, USA

SOURCE: Book of Abstracts, 210th ACS National Meeting, Chicago, IL, August 20-24 (1995), Issue Pt. 2, ORGN-118. American Chemical Society: Washington, D. C.

CODEN: 61XGAC

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Permax r ergolide mesylate) is a semisynthetic ergot alkaloid marketed for the adjunctive treatment of Parkinson's disease. The prior synthesis was a classical linear process that was lengthy in time, and low and variable in yield. The isolation and handling of potent intermediates created a significant exposure hazard from airborne dust. This presentation will describe the development of a one-pot process for the production of pergolide from conception to implementation on industrial scale. This new procedure not only overcomes the problems of low yield and long processing times, but also holds worker exposure to a min. In addition, the highly selective demethylation of quaternized ergoline intermediates that is central to this synthesis suggests broader applicability of this streamlined technol.

L9 ANSWER 193 OF 331 MEDLINE on STN

ACCESSION NUMBER: 1995266329 MEDLINE

DOCUMENT NUMBER: PubMed ID: 7747490

TITLE: Activation by selegiline (Eldepryle) of REM sleep behavior disorder in parkinsonism.

AUTHOR: Louden M B; Morehead M A; Schmidt H S

CORPORATE SOURCE: West Virginia University School of Medicine, Morgantown, USA.

SOURCE: The West Virginia medical journal, (1995 Mar-Apr) Vol. 91, No. 3, pp. 101.

Journal code: 0413777. ISSN: 0043-3284.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CASE REPORTS)

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199506

ENTRY DATE: Entered STN: 21 Jun 1995

Last Updated on STN: 21 Jun 1995

Entered Medline: 9 Jun 1995

AB Abnormal sleep-wake organization is frequently seen in idiopathic parkinsonism (PD) and other parkinsonism syndromes. A 1993 article in The Annals of Neurology first described the high rate of REM behavior disorder (RBD) in non-demented PD patients (1). In this article, we present the case reports of three non-demented PD patients who

manifested RBD while on recommended doses of selegiline (Eldepryle). None of them had problems severe enough to suggest RBD while they were being treated with varying doses of other dopaminergic agents (carbidopa/L-dopa, pergolide) unaccompanied by selegiline.

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ACCESSION NUMBER: 1995146388 EMBASE
TITLE: [Pergolide - A review of its clinical potential].
PERGOLID.
AUTHOR: Poewe, W., Prof. Dr. (correspondence)
CORPORATE SOURCE: Abteilung fur Neurologie, Universitätsklinikum Rudolf Virchow, FU, Augustenburger Platz 1, 13353 Berlin, Germany.
SOURCE: Aktuelle Neurologie, (1995) Vol. 22, No. 2, pp. 71-74.
ISSN: 0302-4350 CODEN: AKNUAR
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: German
SUMMARY LANGUAGE: German; English
ENTRY DATE: Entered STN: 19 Jun 1995
Last Updated on STN: 19 Jun 1995

AB The ergot dopamine agonist pergolide has proved efficacious as an adjunct to L-dopa in advanced Parkinson's disease, as shown by numerous uncontrolled and controlled studies. Most series have demonstrated reductions in L-dopa response fluctuations in the order of 30% or more of total daily off-time and concomitant dose reductions of L-dopa by more than 25%. Preexisting L-dopa dyskinesias may worsen with the addition of pergolide but can frequently be controlled by tapering L-dopa. By virtue of its mixed D1/D2 dopaminergic agonism and a long half-life of more than 8 hours pergolide has theoretical advantages over existing ergot agonists like bromocriptine and lisuride. Although the number of controlled comparative trials is still limited such advantages have also been observed clinically. The available evidence shows that pergolide monotherapy is effective in de novo patients, but there are no data yet to decide whether it can yield more effective long-term monotherapy results in these patients than bromocriptine or lisuride. Similarly there are no clinical data with respect to neuroprotective actions of pergolide shown in animal experiments. The side effects of pergolide are similar to those of other ergot agonists, orthostatic hypotension, nausea and dyskinesias being the most frequent problems. Pergolide is at least as effective an antiparkinsonian agent as lisuride or bromocriptine and may be superior as add-on in patients with late L-dopa failure.

L9 ANSWER 195 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 154
ACCESSION NUMBER: 1995:587011 CAPLUS
DOCUMENT NUMBER: 123:55
ORIGINAL REFERENCE NO.: 123:7a,10a
TITLE: Dopaminergic drugs: pharmacological and therapeutic aspects
AUTHOR(S): Luchsinger, Augusta; Romero, Eduardo; Grilli, Maria; Velasco, Manuel
CORPORATE SOURCE: School of Mediciner Jose Maria Vargas, Universidad Central de Venezuela, Venez.
SOURCE: Progress in Pharmacology and Clinical Pharmacology (1995), 10(2), 69-80
CODEN: PPCPEP; ISSN: 0934-9545

PUBLISHER: Fischer
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 29 refs. It has been widely established that dopamine and its agonists exert an important role in the regulation of the cardiovascular, renal and hormonal systems, acting through adrenergic and beta-adrenergic systems. There are several DA-2 agonists such as bromocriptine, pergolide, lisuride, and lergotrile, which belong to the ergoline family and act both at central and peripheral levels - inhibiting norepinephrine release, which produces a decrease of arterial pressure and, in some cases, such as with bromocriptine and pergolide, a decrease in the heart rate. From a therapeutic viewpoint, the above mentioned DA-2 agonists are widely used for treating Parkinson's disease; these agonists act at the level of DA-2 receptors located in the nigrostriatal system. Bromocriptine and the other mentioned agonists DA-2 are used in the treatment of hyperprolactinemia and in pituitary tumors, since they decrease prolactin secretion and reduce the size of the tumor acting through inhibitory DA-2 receptors located in the tuberoinfundibular system. Similarly, there are also DA-1 agonists such fenoldopam (selective) and piribedil (non selective) which activate peripheral receptors, producing a reduction of peripheral resistance and renal vascular resistance and an increase of renal blood flow. All these effects produce a decrease in arterial pressure and a reflex heart rate increase. Fenoldopam is used in the treatment of arterial hypertension, renal failure, and heart failure. This agonist exerts its action at the level of the DA-1 receptors located in peripheral and renal resistance vessels (which leads to an increase in renal blood flow and a decrease in arterial pressure). Among the selective antagonists of DA-2 receptors, we can mention metoclopramide and domperidone. Both antagonists produce a decrease in the hypotensor response of.

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STN DUPLICATE 155

ACCESSION NUMBER: 1996:66603 BIOSIS
DOCUMENT NUMBER: PREV199698638738
TITLE: Differential effects of three dopamine receptor agonists in MPTP-treated monkeys.
AUTHOR(S): Arai, N.; Isaji, M.; Miyata, H.; Fukuyama, J.; Mizuta, E.; Kuno, S. [Reprint author]
CORPORATE SOURCE: Dep. Neurol. Clin. Res. Cent., Utano Natl. Hosp., Kyoto, Japan
SOURCE: Journal of Neural Transmission Parkinson's Disease and Dementia Section, (1995) Vol. 10, No. 1, pp. 55-62.
ISSN: 0936-3076.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Feb 1996
Last Updated on STN: 10 Feb 1996

AB The behavioral effects of cabergoline, pergolide and bromocriptine were investigated in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-lesioned parkinsonian cynomolgus monkeys with attention to the induction of hyperactivity, as evidenced by irritability, excitability and aggressiveness. All three drugs improved the parkinsonism in a dose-dependent fashion following a single injection. Among the three dopamine (DA) receptor agonists used, the antiparkinsonian effect of pergolide was the strongest and had an immediate effect, while cabergoline showed the longest duration of the antiparkinsonian effect and was least potent in inducing hyperactivity.

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ACCESSION NUMBER: 1995:415059 BIOSIS
DOCUMENT NUMBER: PREV199598429359
TITLE: The Therapeutic Potential of Moclobemide, a Reversible
Selective Monoamine Oxidase A Inhibitor in Parkinson's
disease.
AUTHOR(S): Sieradzan, Katarzyna [Reprint author]; Channon, Shelley;
Ramponi, Cristina; Stern, Gerald M.; Lees, Andrew J.;
Youdim, Moussa B. H.
CORPORATE SOURCE: Dep. Neurol., Manchester Royal Infirmary, Oxford Road,
Manchester, M13, UK
SOURCE: Journal of Clinical Psychopharmacology, (1995)
Vol. 15, No. 4 SUPPL. 2, pp. 51S-59S.
CODEN: JCPYDR. ISSN: 0271-0749.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Sep 1995
Last Updated on STN: 27 Sep 1995

AB Dopamine is equally well deaminated oxidatively by monoamine oxidase (MAO) A and B types. Selegiline (L-deprenyl), a selective inhibitor of MAO-B, ameliorates the "wearing off" akinesia and delays the need for levodopa in mild, previously untreated Parkinson's disease. The therapeutic potential of selective inhibition of MAO-A in Parkinson's disease has not been examined in detail. MAO-A accounts for only about 20% of total MAO activity in the human basal ganglia, and it differs from MAO-B in distribution. In contrast to MAO-B, which is confined to the extraneuronal compartment, MAO-A is found both extraneuronally and within the presynaptic dopaminergic terminals. The inhibition of MAO-A might alter the intraneuronal handling of dopamine reuptaken from synaptic clefts and thereby prolong oral levodopa benefit. We have given moclobemide, a selective, reversible inhibitor of MAO-A, to nondepressed patients with Parkinson's disease receiving standard levodopa/peripheral decarboxylase inhibitor or levodopa with dopaminergic agonist (bromocriptine, pergolide). Selegiline was discontinued at least 8 weeks earlier. A standard oral levodopa challenge was performed at the patient's entry to the study and repeated on the 22nd day of moclobemide treatment (150 mg thrice daily). The overall time spent "on" and "off" before the onset of treatment and during the last week on the drug was estimated from the patients' diaries. Neuropsychological assessments were also made before and after 3 weeks of moclobemide to measure possible effects on cognitive performance and mood. In acute levodopa challenge, the latency of motor response was significantly shortened and its duration was prolonged during moclobemide treatment. Similarly, the Webster's scores in "off" state after overnight withdrawal of dopaminergic medication improved on moclobemide. In nondepressed parkinsonian patients, moclobemide did not alter mood and cognitive measures. The mild symptomatic effect and good tolerance with standard therapy suggest that moclobemide may be a particularly useful antidepressant in Parkinson's disease.

L9 ANSWER 198 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:3005 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 33-11264
TITLE: Pergolide, a new agent for Morbus Parkinson
AUTHOR(S): Peruche, B.; Schulz, M.; et al
CORPORATE SOURCE: Arzneimittelinformationsstelle der ABDA, Ginnheimer-Str.
26, 65760 Eschborn, Germany
SOURCE: Pharmazeutische Zeitung (Germany), (Jul 6 1995)
Vol. 140, pp. 44-45, 48, 50. 19 Refs.

CODEN: PHZIAP. ISSN: 0031-7136.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 95:12484
LANGUAGE: German
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB An overview of pergolide mesylate (Parkotil), an oral antiparkinson agent, is presented, including its chemical classification, pharmacokinetics, mechanisms of action, therapeutic indications, contraindications, drug interactions, adverse effects, and clinical trial data.
Christopher Clancy

L9 ANSWER 199 OF 331 MEDLINE on STN DUPLICATE 157
ACCESSION NUMBER: 1995231724 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7715794
TITLE: Dopamine agonists in Parkinson's disease.
AUTHOR: Wolters E C; Tissingh G; Bergmans P L; Kuiper M A
CORPORATE SOURCE: Postgraduate School of Neuroscience, Department of Neurology, Academic Hospital, Vrije Universiteit, Amsterdam, The Netherlands.
SOURCE: Neurology, (1995 Mar) Vol. 45, No. 3 Suppl 3, pp. S28-34. Ref: 43
Journal code: 0401060. ISSN: 0028-3878.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 24 May 1995
Last Updated on STN: 24 May 1995
Entered Medline: 15 May 1995

AB The main pathologic hallmark of Parkinson's disease is a degeneration of the dopaminergic cells in the substantia nigra, pars compacta and--to a lesser extent--in the ventral tegmental area. Striatal dopamine concentrations are significantly reduced before clinical symptoms become apparent. Recent neuroanatomic and function studies have revealed that the nigrostriatal dopaminergic projection is only one of the neuronal elements integrated into extensive basal ganglia-thalamocortical circuits that are intimately involved in the regulation of motor activity. The possibilities for therapeutic intervention at the level of the different dopamine receptor subtypes and their effect on the regulation of motor behavior will be briefly reviewed. Dopamine precursors are considered to provide the best symptomatic treatment, whereas dopamine agonists, although less effective, might be important in slowing the progression of the disease. Our results with pergolide as monotherapy and in combination therapy in patients with Parkinson's disease also are discussed.

L9 ANSWER 200 OF 331 MEDLINE on STN DUPLICATE 158
ACCESSION NUMBER: 1995231723 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7715793
TITLE: A crossover, controlled study comparing pergolide with bromocriptine as an adjunct to levodopa for the treatment of Parkinson's disease.
AUTHOR: Pezzoli G; Martignoni E; Pacchetti C; Angeleri V; Lamberti P; Muratorio A; Bonuccelli U; De Mari M; Foschi N; Cossutta E; et al
CORPORATE SOURCE: Institute of Clinical Neurology, University of Milan, Italy.

SOURCE: Neurology, (1995 Mar) Vol. 45, No. 3 Suppl 3, pp. S22-7.
 Journal code: 0401060. ISSN: 0028-3878.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: (CLINICAL TRIAL)
 Journal; Article; (JOURNAL ARTICLE)
 (MULTICENTER STUDY)
 (RANDOMIZED CONTROLLED TRIAL)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
 ENTRY MONTH: 199505
 ENTRY DATE: Entered STN: 24 May 1995
 Last Updated on STN: 24 May 1995
 Entered Medline: 15 May 1995

AB A single-blind, crossover study was carried out to compare the efficacy and safety of pergolide against that of bromocriptine in 57 patients with Parkinson's disease who showed a declining response to levodopa therapy. Patients were randomly assigned to receive either bromocriptine followed by pergolide, or pergolide followed by bromocriptine. Both drugs were administered for 12 weeks. Patients were assessed by a clinician blinded to treatment assignment using the New York University Parkinson's Disease Scale. The average daily dose of pergolide was 2.3 +/- 0.8 mg and of bromocriptine 24.2 +/- 8.4 mg. Addition of pergolide or bromocriptine resulted in a significant improvement in total scores when compared with the previous treatment of levodopa alone (pergolide, $p = 0.0001$; bromocriptine, $p = 0.0005$). Pergolide was more effective than bromocriptine in daily living scores ($p = 0.02$) and motor scores ($p = 0.038$). No differences in the incidence of dyskinesias, dystonias, or psychosis were observed between groups. Fewer adverse events were recorded in the pergolide group, and most patients and physicians preferred pergolide to bromocriptine. Pergolide as adjunctive therapy to levodopa was more effective than bromocriptine in this short-term trial.

L9 ANSWER 201 OF 331 MEDLINE on STN DUPLICATE 159
 ACCESSION NUMBER: 1995231722 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 7715792
 TITLE: Pergolide in the treatment of Parkinson's disease.
 AUTHOR: Mizuno Y; Kondo T; Narabayashi H
 CORPORATE SOURCE: Department of Neurology, Juntendo University School of Medicine, Tokyo, Japan.
 SOURCE: Neurology, (1995 Mar) Vol. 45, No. 3 Suppl 3, pp. S13-21.
 Journal code: 0401060. ISSN: 0028-3878.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: (CLINICAL TRIAL)
 Journal; Article; (JOURNAL ARTICLE)
 (MULTICENTER STUDY)
 (RANDOMIZED CONTROLLED TRIAL)
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
 ENTRY MONTH: 199505
 ENTRY DATE: Entered STN: 24 May 1995
 Last Updated on STN: 24 May 1995
 Entered Medline: 15 May 1995

AB Three trials evaluated the efficacy and safety of pergolide. Eighty-six de novo patients and 314 patients already receiving levodopa were enrolled in an open-label study. Of the de novo patients, 47.5% showed a marked or moderate improvement and 32% showed a mild improvement. In the levodopa add-on group, 53.8% showed marked or moderate improvement

and 36.3% showed mild improvement. In a short-term, double-blind study, the efficacy of pergolide was compared with that of bromocriptine. One hundred seventy-two patients were randomized to receive pergolide, and 173 were randomized to receive bromocriptine. In de novo patients, bromocriptine (n = 49) and pergolide (n = 49) demonstrated similar efficacy. However, significantly more levodopa-treated patients in the pergolide group, compared with the bromocriptine group, demonstrated marked or moderate improvements in several items of the rating scale score. In a long-term study, 151 of 314 patients receiving pergolide in combination with levodopa remained in the study for 3 years, and 127 for 4 years, and in these patients the initial improvement was maintained. In 18 of 62 de novo patients, the initial improvement was maintained for up to 3 years. These trials indicate that pergolide has efficacy in patients with Parkinson's disease, either as monotherapy or in combination with levodopa.

L9 ANSWER 202 OF 331 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation
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ACCESSION NUMBER: 1995:274401 SCISEARCH

THE GENUINE ARTICLE: QT862

TITLE: THE RATIONALE FOR THE USE OF DOPAMINE AGONISTS IN
PARKINSONS-DISEASE

AUTHOR: JENNER P (Reprint)

CORPORATE SOURCE: UNIV LONDON KINGS COLL, NEURODEGENERAT DIS RES CTR, DIV
BIOMED SCI, PHARMACOL GRP, MANRESA RD, LONDON SW3 6LX,
ENGLAND (Reprint)

COUNTRY OF AUTHOR: ENGLAND

SOURCE: NEUROLOGY, (MAR 1995) Vol. 45, No. 3, Supp. [3],
pp. 6-12.

ISSN: 0028-3878.

PUBLISHER: LITTLE BROWN CO, 34 BEACON STREET, BOSTON, MA 02108-1493.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE; CLIN

LANGUAGE: English

REFERENCE COUNT: 51

ENTRY DATE: Entered STN: 1995

Last Updated on STN: 1995

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Experimental and clinical studies indicate that both dopamine D-2-like and D-1-like receptors are important in reversing the motor symptoms of Parkinson's disease, and therefore stimulation of both D-1 and D-2 receptors may be advantageous in its treatment. At present, the role of other receptor subtypes, such as the D-3 receptor, remains unknown, although in primates the D-3 receptor might be of importance because it exists in significant amounts within the caudate-putamen. Both D-1 and D-2 agonists induce dyskinesias in drug-naïve, MPTP-treated primates and provoke dyskinesias in levodopa-primed animals. D-1 agonists in low doses, however, might have antiparkinsonian effects without inducing dyskinesias, and on repeated administration perhaps can diminish the intensity of dyskinesias in levodopa-primed, MPTP-treated primates. The production of dyskinesias in Parkinson's disease might reflect an imbalance in the D-1-direct and D-2-indirect GABAergic output pathways from the caudate-putamen, which colocalize tachykinins and enkephalins, respectively. Destruction of the nigrostriatal pathway decreases the mRNA for substance P but elevates the mRNA for enkephalin. Treatment with levodopa reverses the decrease in substance P mRNA but has either a partial or no effect on mRNA for enkephalin. This suggests that levodopa treatment leads to a new imbalance between output from the striatum through the direct and indirect pathways. In contrast, dopamine agonists appear less able than levodopa to manipulate basal ganglia outflow. This

might reflect their decreased ability to reverse parkinsonian motor deficits or the greater ability of levodopa to provoke dyskinesias. Dopamine agonist drugs also might exert neuroprotective actions. Pergolide, like selegiline, elevates superoxide dismutase activity in brain, decreases hydrogen peroxide formation from dopamine, and preserves nigral cells in aging rats. Bromocriptine, apomorphine, and other agonists also scavenge free radicals and show antioxidant activity, compared with the mainly pro-oxidant actions of levodopa.

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ACCESSION NUMBER: 1995243051 EMBASE

TITLE: The therapeutic potential of moclobemide, a reversible selective monoamine oxidase A inhibitor in Parkinson's disease.

AUTHOR: Sieradzan, K., Dr. (correspondence); Channon, S.; Ramponi, C.; Stern, G.M.; Lees, A.J.; Youdim, M.B.H.

CORPORATE SOURCE: Department of Neurology, Manchester Royal Infirmary, Oxford Road, Manchester M13, United Kingdom.

SOURCE: Journal of Clinical Psychopharmacology, (1995)
Vol. 15, No. 4 SUPPL. 2, pp. 51S-59S.
ISSN: 0271-0749 CODEN: JCPYDR

COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article; (Conference paper)

FILE SEGMENT: 020 Gerontology and Geriatrics

030 Clinical and Experimental Pharmacology

032 Psychiatry

037 Drug Literature Index

008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 6 Sep 1995

Last Updated on STN: 6 Sep 1995

AB Dopamine is equally well deaminated oxidatively by monoamine oxidase (MAO) A and B types. Selegiline (L-deprenyl), a selective inhibitor of MAO-B, ameliorates the 'wearing off' akinesia and delays the need for levodopa in mild, previously untreated Parkinson's disease. The therapeutic potential of selective inhibition of MAO-A in Parkinson's disease has not been examined in detail. MAO-A accounts for only about 20% Of total MAO activity in the human basal ganglia, and it differs from MAO-B in distribution. In contrast to MAO-B, which is confined to the extraneuronal compartment, MAO-A is found both extraneuronally and within the presynaptic dopaminergic terminals. The inhibition of MAO-A might alter the intraneuronal handling of dopamine reuptaken from synaptic clefts and thereby prolong oral levodopa benefit. We have given moclobemide, a selective, reversible inhibitor of MAO-A, to nondepressed patients with Parkinson's disease receiving standard levodopa/peripheral decarboxylase inhibitor or levodopa with dopaminergic agonist (bromocriptine, pergolide). Selegiline was discontinued at least 8 weeks earlier. A standard oral levodopa challenge was performed at the patient's entry to the; study and repeated on the 22nd day of moclobemide treatment (150 mg thrice daily). The overall timespent 'on' and 'off' before the onset of treatment and during the last week on the drug was estimated from the patients' diaries. Neuropsychological assessments were also made before and after 3 weeks of moclobemide to measure possible effects on cognitive performance and mood. In acute levodopa challenge, the latency of motor response was significantly shortened and its duration was prolonged during moclobemide treatment. Similarly, the Webster's scores in 'off' state after overnight withdrawal of dopaminergic medication improved on moclobemide. In nondepressed parkinsonian patients, moclobemide did not alter mood and cognitive measures. The mild symptomatic effect and good tolerance with

standard therapy suggest that moclobemide may be a particularly useful antidepressant in Parkinson's disease.

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ACCESSION NUMBER: 1995:86924 BIOSIS
DOCUMENT NUMBER: PREV199598101224
TITLE: Reproductive and Developmental Toxicity of the Dopamine
Agonist Pergolide Mesylate in Mice.
AUTHOR(S): Hoyt, J. A. [Reprint author]; Byrd, R. A.; Owen, N. V.
CORPORATE SOURCE: Toxicol. Res. Lab., Lilly Res. Lab., 2001 W. Main St., PO
Box 708, Greenfield, IN 46140, USA
SOURCE: Arzneimittel-Forschung, (1994) Vol. 44, No. 11,
pp. 1177-1183.
CODEN: ARZNAD. ISSN: 0004-4172.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Feb 1995
Last Updated on STN: 23 Feb 1995

AB Pergolide (Permax, LY127809, CAS 66104-23-2) a dopamine agonist for the treatment of Parkinson's disease, was evaluated for reproductive and developmental toxicity. Pergolide was administered in the diet at levels of 0, 5, 15, or 50 ppm to male and female ICR mice. In the F-0 generation, the males were treated for 9 weeks prior to mating and throughout mating. The females were treated for 2 weeks prior to mating and throughout mating, gestation, and lactation (postnatal segment only). Females assigned to the teratology segment were killed on gestation day 18 for evaluation of fetal viability, weights, and morphology. Females assigned to the postnatal component were allowed to deliver and maintain their offspring throughout a 21-day lactation period. One male and one female were selected from each litter to continue as the F-1 generation. Possible exposure of the F-1 generation to pergolide ended at weaning. Growth of the F-1 animals was monitored and reproductive performance evaluated. Treatment-related effects in the F-0 generation were consistent with the pharmacologic effects of a dopamine agonist. These effects included pregnancy blockage at the 50-ppm dietary level and dose-related body weight depression in lactating dams and suckling progeny at the 15- and 50-ppm dietary levels. An increase in progeny mortality at the 50-ppm dietary level was attributed to lactation failure of the treated dams. The F-1 mice of the 15- and 50-ppm groups remained smaller than the control mice until termination at approximately 20 weeks of age, although weight gains following weaning were not depressed and no impairment of mating performance or fertility was observed. In this study, the no-adverse-effect-level was the 5-ppm dietary level which was equivalent to approximately 0.5 mg/kg/day of pergolide mesylate.

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ACCESSION NUMBER: 1994250047 EMBASE
TITLE: Pergolide compared with bromocriptine in Parkinson's disease: A multicenter, crossover, controlled study.
AUTHOR: Pezzoli, G., Dr. (correspondence); Martignoni, E.;
Pacchetti, C.; Angeleri, V.A.; Lamberti, P.; Muratorio, A.;
Bonuccelli, U.; De Mari, M.; Foschi, N.; Cossutta, E.;
Nicoletti, F.; Giammona, F.; Canesi, M.; Scarlato, G.;
Caraceni, T.; Moscarelli, E.
CORPORATE SOURCE: Osped Maggiore Policlinico Pad Ponti, Institute of Clinical
Neurology, via F Sforza 35, I 20122 Milan, Italy.
SOURCE: Movement Disorders, (1994) Vol. 9, No. 4, pp.
431-436.
ISSN: 0885-3185 CODEN: MOVDEA

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 26 Aug 1994
Last Updated on STN: 26 Aug 1994

AB We compared the efficacy and safety of pergolide and bromocriptine in 57 patients with Parkinson's disease (PD) with a declining response to levodopa therapy in a single-blind, crossover study. Patients were placed randomly on the sequence bromocriptine- pergolide (12 + 12 weeks) or vice versa. Regular evaluations using the New York University Parkinson's Disease Scale were performed by a clinician blinded to treatment assignment. Patients' and clinicians' impressions also were recorded. The average daily dose of pergolide was 2.3 + 0.8 mg, and that of bromocriptine was 24.2 + 8.4 mg. Significantly greater efficacy was demonstrated by both drugs as adjunctive therapy to levodopa compared with previous treatment of levodopa alone (pergolide, $p = 0.0001$; bromocriptine, $p = 0.0005$; Wilcoxon t test). Pergolide was more effective than bromocriptine in daily living scores ($p = 0.020$) and motor scores ($p = 0.038$). No difference in dyskinesias, dystonias, and psychosis was observed. Adverse events were more frequent in bromocriptine-treated patients. Most patients and physicians preferred pergolide to bromocriptine. Pergolide as adjunctive therapy to levodopa was more effective than bromocriptine in this short-term trial.

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ACCESSION NUMBER: 1994195651 EMBASE
TITLE: [Parkinson's disease - Latest scientific findings of pathogenesis and therapy].
MORBUS PARKINSON. AKTUELLE ERKENNTNISSE ZU PATHOGENESE UND THERAPIE.
AUTHOR: Poewe, W., Prof. Dr. (correspondence)
CORPORATE SOURCE: Abt. f. Neurologie, Universitätsklinikum Rudolf Virchow, EV, Augustenburger Platz 1, 13353 Berlin, Germany.
SOURCE: TW Neurologie Psychiatrie, (1994) Vol. 8, No. 6, pp. 284-288.
ISSN: 0935-3224 CODEN: TWNPE3
COUNTRY: Germany
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: German
SUMMARY LANGUAGE: German; English
ENTRY DATE: Entered STN: 3 Aug 1994
Last Updated on STN: 3 Aug 1994

AB The etiopathogenesis of Parkinson's disease remains obscure, but mechanisms of oxidative stress and mitochondrial energy failure are likely to play a role. Although there is no proof for any of them being primary causal events of nigral cell death, their identification has greatly stimulated efforts to develop neuroprotective treatment strategies. Antioxydants like Deprenyl have not proven to be unequivocally capable to exert protective effects beyond their symptomatic actions. Recent speculations about neuroprotective properties also involve other symptomatic agents like the dopamine agonist pergolide or the amantadines, because of their weak NMDA-antagonistic properties. While neuroprotection remains a far goal, there are some promising new developments in the field of symptomatic antiparkinsonian

therapy. These include the combined use of L-Dopa with a COMT inhibitor or new surgical techniques of stereotactic pallidotomy to relieve both akinesia and preexisting drug-induced dyskinesias.

L9 ANSWER 207 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 162
ACCESSION NUMBER: 1994:570393 CAPLUS
DOCUMENT NUMBER: 121:170393
ORIGINAL REFERENCE NO.: 121:30679a,30682a
TITLE: Preclinical toxicology studies with the new dopamine agonist pergolide: acute, subchronic, and chronic evaluations
AUTHOR(S): Francis, P. C.; Carlson, K. H.; Owen, N. V.; Adams, E. R.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly Co., Greenfield, IN, USA
SOURCE: Arzneimittel-Forschung (1994), 44(3), 278-84
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pergolide (LY127809, CAS 66104-23-2), a dopamine agonist for the treatment of Parkinson's disease, was evaluated for toxicity in acute, subchronic, and chronic studies. Acute toxicity tests using oral, i.v. and i.p. routes were conducted in rats, mice, rabbits, and dogs. The acute oral median LDs (MLD) ranged from 8.4 to 33.6 mg/kg in Wistar and Fischer 344 rats, and from 54.0 to 87.2 mg/kg in ICR mice. Oral doses of 20 and 25 mg/kg produced no mortality in rabbits or dogs, resp. The MLD by the i.v. route ranged from 0.59 to 0.87 mg/kg for Fischer 344 rats and from 11.6 to 37.1 mg/kg for ICR mice. The predominant signs of toxicity in the acute studies included hyperactivity; poor grooming, ptosis, aggressive behavior, increased gnawing activity, tremors, convulsions, and emesis. In the subchronic and chronic studies. Fischer 344 rats, B6C3F1 mice, and beagle dogs were administered pergolide either by gavage or in the diet for up to 1 yr. Daily doses in these studies ranged up to 20 mg/kg for rats, 45 mg/kg for mice, and 5 mg/kg for dogs. The predominant treatment = related effects seen in these studies were attributable to the pharmacol. activity of pergolide. These consisted primarily of CNS-mediated clin. signs in rats and dogs, weight loss or decreased weight gain, emesis in dogs, and inhibition of lysis of corpora lutea with a corresponding increase in the weight of the uterus and ovaries. Pergolide treatment was not associated with any specific target organ toxicity. Decreased erythrocytic parameters and increased serum enzyme values seen in the repeated-dose studies were considered to be secondary responses to the effects on body weight. In the 1-yr studies with rats and dogs, the no-observed-adverse-effect levels (NOAEL) were 0.06 and 0.1 mg/kg, resp.

L9 ANSWER 208 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 163
ACCESSION NUMBER: 1994356903 EMBASE
TITLE: Neuroprotection by dopamine agonists.
AUTHOR: Lange, K.W., Prof. Dr. (correspondence); Rausch, W.-D.; Gsell, W.; Naumann, M.; Oestreicher, E.; Riederer, P.
CORPORATE SOURCE: Institute of Psychology, University of Freiburg, P.O. Box, D-79085 Freiburg/Br., Germany.
SOURCE: Journal of Neural Transmission, Supplement, (1994) No. 43, pp. 183-201.
ISSN: 0303-6995 CODEN: JNTSD4
COUNTRY: Austria
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 29 Dec 1994

Last Updated on STN: 29 Dec 1994

AB Research of Parkinson's disease has led to new hypotheses concerning the mechanisms of neurodegeneration and to the development of neuroprotective agents. Recent findings of impaired mitochondrial function, altered iron metabolism and increased lipid peroxidation in the substantia nigra of parkinsonian patients emphasize the significance of oxidative stress and free radical formation in the pathogenesis of Parkinson's disease. Present research is therefore focussing on improvements in neuroprotective therapy to prevent or slow the rate of progression of the disease. Possible neuroprotective strategies include free radical scavengers, monoamine oxidase-B inhibitors, iron chelators and glutamate antagonists. Recent studies point to the possibility of achieving neuroprotection in ageing and parkinsonism by the administration of dopamine agonist. In the rat, the dopamine agonist pergolide appears to preserve the integrity of nigrostriatal neurones with ageing. The prevention of age-related degeneration may be achieved as a result of a decreased dopamine turnover and reduced conversion of dopamine to toxic compounds. In our own study, bromocriptine treatment prevented the striatal dopamine reduction following MPTP administration in the mouse. These results suggest that the neurotoxic effects of MPTP can be prevented by bromocriptine. Monotherapy with the dopamine agonist lisuride in the early stages of Parkinson's disease delays the need for the initiation of levodopa treatment to a similar extent as has been reported for L-deprenyl. It remains to be shown whether this is due to neuroprotective efficacy of the dopamine agonist or to a direct symptomatic effect.

L9 ANSWER 209 OF 331 MEDLINE on STN DUPLICATE 164
ACCESSION NUMBER: 1994203934 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8153048
TITLE: Treatment of Parkinson's disease. From theory to practice.
AUTHOR: Ahlskog J E
CORPORATE SOURCE: Department of Neurology, Mayo Clinic, Rochester, MN 55905.
SOURCE: Postgraduate medicine, (1994 Apr) Vol. 95, No. 5,
pp. 52-4, 57-8, 61-4 passim. Ref: 25
Journal code: 0401147. ISSN: 0032-5481.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 23 May 1994
Last Updated on STN: 23 May 1994
Entered Medline: 10 May 1994

AB Parkinson's disease responds rather dramatically to levodopa therapy during the first several years of treatment. With advancing disease, however, symptom control becomes more erratic, and some symptoms may become refractory to treatment. The use of selegiline hydrochloride (Eldepryl) has been proposed to slow the progression of Parkinson's disease; however, current evidence suggests that it is only partially effective at best, and there is no definite proof of a neuroprotective effect. Nonetheless, it is a reasonable treatment choice. Carbidopa-levodopa (Sinemet) remains the foundation of symptomatic treatment of Parkinson's disease. Clinical fluctuations occurring with advancing disease may be at least partially controlled by appropriate adjustments in dosage. A direct-acting dopamine agonist, bromocriptine mesylate (Parlodel) or pergolide mesylate (Permax), can be very helpful as adjunctive therapy to smooth these

clinical fluctuations. Excessive intracellular oxidative stress has been proposed as a cause of Parkinson's disease; however, a recent multicenter trial investigating the use of high doses of the antioxidant vitamin E showed it to be ineffective. Whether other forms of nonspecific antioxidant therapy will prove beneficial is open to speculation.

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ACCESSION NUMBER: 1994031004 EMBASE
TITLE: A multicenter double-blind placebo-controlled trial of pergolide as an adjunct to sinemet® in Parkinson's disease.
AUTHOR: Olanow, C.W., Dr. (correspondence); Fahn, S.; Muentner, M.; Klawans, H.; Hurtig, H.; Stern, M.; Shoulson, I.; Kurlan, R.; Grimes, J.D.; Jankovic, J.; Hoehn, M.; Markham, C.H.; Duvoisin, R.; Reinmuth, O.; Leonard, H.A.; Ahlskog, E.; Feldman, R.; Hershey, L.; Yahr, M.D.
CORPORATE SOURCE: Dept of Neurology and Pharmacology, University of South Florida, Tampa, FL, United States.
SOURCE: Movement Disorders, (1994) Vol. 9, No. 1, pp. 40-47.
ISSN: 0885-3185 CODEN: MOVDEA
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 6 Feb 1994
Last Updated on STN: 6 Feb 1994

AB Three hundred and seventy-six subjects with advanced Parkinson's disease participated in a prospective, double-blind placebo-controlled study of the dopamine agonist pergolide mesylate as an adjunct to Sinemet®. At 6 months, patients randomized to pergolide had a statistically significant improvement in total Parkinson's score, scores of activities of daily living, motor function, number of 'off' hours, Hoehn and Yahr stage, and numerous parameters of parkinsonian function including bradykinesia, rigidity, gait, and dexterity. This benefit was obtained with the addition of a mean dose of 2.94 mg of pergolide, which permitted a 24.7% reduction in dose of levodopa. Adverse reactions were, for the most part, mild, reversible, and not of major clinical significance. No significant cardiac or electrocardiographic abnormalities were detected. This study demonstrates that pergolide mesylate, as an adjunct to levodopa, is an effective antiparkinsonian agent that provides clinical improvement while permitting a reduction in levodopa dose.

L9 ANSWER 211 OF 331 MEDLINE on STN DUPLICATE 166
ACCESSION NUMBER: 1994323057 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7914010
TITLE: Initiating treatment for idiopathic parkinsonism.
AUTHOR: Calne D B
CORPORATE SOURCE: Department of Medicine, University of British Columbia, Vancouver, Canada.
SOURCE: Neurology, (1994 Jul) Vol. 44, No. 7 Suppl 6, pp. S19-22. Ref: 10
Journal code: 0401060. ISSN: 0028-3878.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)

LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 9 Sep 1994
Last Updated on STN: 6 Feb 1995
Entered Medline: 26 Aug 1994

AB The initial decision in the management of idiopathic parkinsonism is whether any pharmacotherapy is indicated. There is no conclusive evidence that treatment is helpful before symptoms start to affect the patient's life, although some neurologists believe that deprenyl, also known as selegiline, could be useful. Once functional deficits begin to interfere with the patient's work or social activities, treating symptoms becomes appropriate. Anticholinergics and amantadine can be used, but their limited benefit is often accompanied by unacceptable adverse effects. Dopaminomimetics are the most satisfactory medications, including levodopa and such artificial dopamine agonists as bromocriptine, pergolide, or lisuride.

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STN DUPLICATE 167

ACCESSION NUMBER: 1995:83090 BIOSIS
DOCUMENT NUMBER: PREV199598097390
TITLE: Early idiopathic parkinsonism: Initiation and optimization of treatment.
AUTHOR(S): Calne, Donald B.
CORPORATE SOURCE: Neurodegenerative Disorders Cent., Faculty Med., Vancouver Hosp., Purdy Pavillion, 2211 Westbrook Mall, Vancouver, BC V6T 2B5, Canada
SOURCE: Clinical Neuropharmacology, (1994) Vol. 17, No. SUPPL. 2, pp. S14-S18.
CODEN: CLNEDB. ISSN: 0362-5664.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Feb 1995
Last Updated on STN: 23 Feb 1995

AB Once a diagnosis of idiopathic parkinsonism has been made, the choice and timing of therapy depend almost entirely on the patient's need for symptomatic relief, as no presently available therapy has any effect on the pathogenesis of the disease. Five categories of drugs are available for the treatment of idiopathic parkinsonism. Anticholinergic agents are effective against tremor but have prominent adverse effects. Amantadine has similar effects but is more active against rigidity and bradykinesia. Selegiline is a monoamine oxidase-B inhibitor: once thought to affect the pathogenesis of idiopathic parkinsonism, it is now known to offer only symptomatic relief. The dopamine agonists (bromocriptine, pergolide, and lisuride) stimulate D-2 receptors: they have antiparkinsonian effects and tolerance profiles broadly similar to those of levodopa but are slightly less efficacious. Pleural effusions and pulmonary fibrosis are unusual but important complications of these drugs: chest x-ray examinations are therefore recommended for all patients starting such treatment. Levodopa (combined with an extracerebral decarboxylase inhibitor to prevent nausea, the main adverse effect) has become the standard antiparkinsonism treatment. Patients using this preparation can suffer considerable variations in mobility and dyskinesia, which may be related to rapid, large-scale oscillations in plasma levodopa concentrations. Controlled-release (CR) preparations have been developed in an attempt to minimize these fluctuations and reduce long-term side effects. There is no universally agreed treatment for idiopathic parkinsonism. However, experience shows that a good balance of antiparkinsonian activity and adverse effects can be obtained by initiating treatment with a combination of levodopa and a decarboxylase inhibitor. A dopamine

agonist can be added if the disease progresses and increased therapeutic activity is required.

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ACCESSION NUMBER: 1994:165810 BIOSIS
DOCUMENT NUMBER: PREV199497178810
TITLE: An analysis of treatment options and outcome in patients
with Parkinson's disease and severe dyskinesias.
AUTHOR(S): Mark, Margery H.,; Sage, Jacob I. [Reprint author]
CORPORATE SOURCE: Dep. Neurol., UMDNJ-Robert Wood Johnson Med. Sch., CN-19,
New Brunswick, NJ 08903, USA
SOURCE: Annals of Clinical and Laboratory Science, (1994)
Vol. 24, No. 1, pp. 12-21.
CODEN: ACLSCP. ISSN: 0091-7370.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Apr 1994
Last Updated on STN: 10 Apr 1994

AB Forty-one patients with Parkinson's disease and severe
dyskinesias were analyzed retrospectively to determine if some general
principles would emerge to aid physicians handling this complication of
treatment. Dyskinesia type (high dopa chorea (HDC), low dopa chorea
(LDC), high dopa dystonia (HDD), and low dopa dystonia (LDD)) predicted
response to treatment and whether or not levodopa dose reduction would
benefit dyskinesias without producing unacceptable "offs." High dopa
chorea improved best but at the expense of increased "off" time, followed
by LDD, HDD, and LDC. Levodopa reduction was an acceptable strategy in
ameliorating HDC and LDD only. Adjunctive therapy benefitted all
dyskinesia types, although the majority of patients (12/17) helped by
selegiline had LDD or LDC. Generally, low doses of dopamine agonists were
helpful (bromocriptine lt 20 mg/day; pergolide lt 2 mg/day).
When adding adjunctive therapy (except for selegiline or
controlled-release carbidopa/levodopa), concomitant reduction in daily
dose of levodopa was not an effective strategy to decrease dyskinesias.
Serial trials of multiple drug regimens are useful in these patients.

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ACCESSION NUMBER: 1994119237 EMBASE
TITLE: Treatment of Parkinson's disease: From theory to practice.
AUTHOR: Ahlskog, J.E., Dr. (correspondence)
CORPORATE SOURCE: Department of Neurology, Mayo Clinic, Rochester, MN 55905,
United States.
SOURCE: Postgraduate Medicine, (1994) Vol. 95, No. 5, pp.
52-54+57-58+61-64+68-69.
ISSN: 0032-5481 CODEN: POMDAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 May 1994
Last Updated on STN: 11 May 1994

AB Parkinson's disease responds rather dramatically to levodopa
therapy during the first several years of treatment. With advancing
disease, however, symptom control becomes more erratic, and some symptoms
may become refractory to treatment. The use of selegiline hydrochloride
(Eldepryl) has been proposed to slow the progression of Parkinson
's disease; however, current evidence suggests that it is only partially
effective at best, and there is no definite proof of a neuroprotective

effect. Nonetheless, it is a reasonable treatment choice. Carbidopa-levodopa (Sinemet) remains the foundation of symptomatic treatment of Parkinson's disease. Clinical fluctuations occurring with advancing disease may be at least partially controlled by appropriate adjustments in dosage. A direct-acting dopamine agonist, bromocriptine mesylate (Parlodel) or pergolide mesylate (Permax), can be very helpful as adjunctive therapy to smooth these clinical fluctuations. Excessive intracellular oxidative stress has been proposed as a cause of Parkinson's disease; however, a recent multicenter trial investigating the use of high doses of the antioxidant vitamin E showed it to be ineffective. Whether other forms of nonspecific antioxidant therapy will prove beneficial is open to speculation.

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ACCESSION NUMBER: 1994376272 EMBASE
TITLE: Early idiopathic parkinsonism: Initiation and optimization of treatment.
AUTHOR: Calne, D.B., Dr. (correspondence)
CORPORATE SOURCE: Neurodegenerative Disorders Centre, Faculty of Medicine, Vancouver Hospital, Vancouver, BC V6T 2B5, Canada.
SOURCE: Clinical Neuropharmacology, (1994) Vol. 17, No. SUPPL. 2, pp. S14-S18.
ISSN: 0362-5664 CODEN: CLNEDB
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 18 Jan 1995
Last Updated on STN: 18 Jan 1995

AB Once a diagnosis of idiopathic parkinsonism has been made, the choice and timing of therapy depend almost entirely on the patient's need for symptomatic relief, as no presently available therapy has any effect on the pathogenesis of the disease. Five categories of drugs are available for the treatment of idiopathic parkinsonism. Anticholinergic agents are effective against tremor but have prominent adverse effects. Amantadine has similar effects but is more active against rigidity and bradykinesia. Selegiline is a monoamine oxidase-B inhibitor; once thought to affect the pathogenesis of idiopathic parkinsonism, it is now known to offer only symptomatic relief. The dopamine agonists (bromocriptine, pergolide, and lisuride) stimulate D(2) receptors; they have antiparkinsonian effects and tolerance profiles broadly similar to those of levodopa but are slightly less efficacious. Pleural effusions and pulmonary fibrosis are unusual but important complications of these drugs; chest x-ray examinations are therefore recommended for all patients starting such treatment. Levodopa (combined with an extracerebral decarboxylase inhibitor to prevent nausea, the main adverse effect) has become the standard antiparkinsonism treatment. Patients using this preparation can suffer considerable variations in mobility and dyskinesia, which may be related to rapid, large-scale oscillations in plasma levodopa concentrations. Controlled-release (CR) preparations have been developed in an attempt to minimize these fluctuations and reduce long-term side effects. There is no universally agreed treatment for idiopathic parkinsonism. However, experience shows that a good balance of antiparkinsonian activity and adverse effects can be obtained by initiating treatment with a combination of levodopa and a decarboxylase inhibitor. A dopamine agonist can be added if the disease progresses and increased therapeutic activity is required.

L9 ANSWER 216 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 169
 ACCESSION NUMBER: 1993:574219 CAPLUS
 DOCUMENT NUMBER: 119:174219
 ORIGINAL REFERENCE NO.: 119:30931a,30932a
 TITLE: ergot alkaloid compositions for treatment of
 degenerative or ischemic neurological diseases
 INVENTOR(S): Poli, Stefano; Mailland, Federico; Coppi, Germano
 PATENT ASSIGNEE(S): Poli Industria Chimica S.p.A., Italy
 SOURCE: Ger. Offen., 8 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4240798	A1	19930609	DE 1992-4240798	19921201 <--
ES 2109114	A1	19980101	ES 1992-2439	19921201 <--
ES 2109114	B1	19980616		

PRIORITY APPLN. INFO.: IT 1991-MI3241 A 19911203
 AB The title compns., which protect cerebral neurons from endogenous and
 exogenous toxic substances, comprise clavines (nicergoline, lergotrile,
 pergolide), lysergamides (bromocriptine, dihydroergocristine,
 dihydroergotocine, β -dihydroergocryptine), and
 8 α -aminoergolines (lisuride, terguride). Thus, bromocriptine (2
 mg/kg/day) partially counteracted the parkinsonism-like symptoms
 in monkeys caused by MPTP (0.2 mg/kg i.v.). A lyophilized preparation in an
 ampul contained nicergoline 4, tartaric acid 1.04, and lactose 30 mg.
 OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD
 (6 CITINGS)

L9 ANSWER 217 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights
 reserved on STN DUPLICATE 170
 ACCESSION NUMBER: 1993292131 EMBASE
 TITLE: Current status of dopamine agonists in Parkinson's disease
 management.
 AUTHOR: Montastruc, J.L., Prof. (correspondence); Rascol, O.;
 Senard, J.M.
 CORPORATE SOURCE: Lab Pharmacologie Medicale/Clinique, INSERM U317, Faculte
 de Medecine, 37 allees Jules Guesde, 31073 Toulouse Cedex,
 France.
 SOURCE: Drugs, (1993) Vol. 46, No. 3, pp. 384-393.
 ISSN: 0012-6667 CODEN: DRUGAY
 COUNTRY: New Zealand
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 31 Oct 1993
 Last Updated on STN: 31 Oct 1993
 AB The occurrence of late side effects of long term levodopa therapy
 (fluctuations in motor performance, abnormal movements, and symptoms
 unresponsive to dihydroxyphenylalanine) led the search for novel anti-
 Parkinsonian drugs. Dopamine agonists are one of the newer
 families of anti-Parkinsonian agents, and they include ergot
 derivatives and apomorphine, which can be used in the different stages of
 Parkinson's disease. Ergot derivatives (bromocriptine, lisuride,
 pergolide) are believed to act independently of the dying cells of

the substantia nigra, acting instead directly on postsynaptic dopamine receptors in the striatum. They are usually used in combination with levodopa when late side effects occur. especially 'wearing-off' or decreased efficacy of levodopa. They can also be prescribed earlier in combination with levodopa in de novo Parkinsonian patients, and in this setting are thought delay the occurrence of late adverse motor effects. In some patients, monotherapy with relatively high doses of ergot derivatives can be used as initial treatment. However, their efficacy often decreases after 1 to 3 years, thus justifying a late combination with levodopa. Apomorphine is a non-ergot derivative dopamine agonist, which is used subcutaneously for the treatment of severe 'off' refractory periods, in combination with other dopaminergic drugs without changing the patient's routine drug regimen.

L9 ANSWER 218 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 171
ACCESSION NUMBER: 1993:492440 CAPLUS
DOCUMENT NUMBER: 119:92440
ORIGINAL REFERENCE NO.: 119:16605a,16608a
TITLE: Hydroxyl free radical (\cdot OH) formation reflected by salicylate hydroxylation and neuromelanin: in vivo markers for oxidant injury of nigral neurons
AUTHOR(S): Chiueh, C. C.; Murphy, D. L.; Miyake, H.; Lang, K.; Gramsbergen, Jan Ebert P.; Huang, S. J.
CORPORATE SOURCE: Lab. Clin. Sci., Natl. Inst. Ment. Health, Bethesda, MD, 20892, USA
SOURCE: Annals of the New York Academy of Sciences (1993), 679 (Markers of Neuronal Injury and Degeneration), 370-5
CODEN: ANYAA9; ISSN: 0077-8923
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 20 refs. Oxidant stress elicited by reactive O species generated by metal-catalyzed dopamine autoxidn. may be the common neurodegenerative process involved in selective nigrostriatal degeneration in Parkinson's disease produced by environmental neurotoxins such as manganese and compds. related to 6-hydroxydopamine as well as MPTP. By investigating pathophysiol. roles of \cdot OH free radicals in the central nervous system, researchers may be able to answer some of clin. questions concerning the use of neuroprotective agents (i.e., deprenyl, nimodipine, pergolide and lazaroïd) to halt or treat progressive neurodegenerative brain disorders.
OS.CITING REF COUNT: 24 THERE ARE 24 CAPLUS RECORDS THAT CITE THIS RECORD (24 CITINGS)

L9 ANSWER 219 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 172
ACCESSION NUMBER: 1993251624 EMBASE
TITLE: Strategies in the treatment of early Parkinson's disease.
AUTHOR: Rinne, U.K. (correspondence)
CORPORATE SOURCE: Department of Neurology, University of Turku, SF-20520 Turku, Finland.
SOURCE: Acta Neurologica Scandinavica, Supplement, (1993) Vol. 87, No. 146, pp. 50-53.
ISSN: 0065-1427 CODEN: ANSLAC
COUNTRY: Denmark
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 26 Sep 1993
Last Updated on STN: 26 Sep 1993

AB Over recent years I have been studying whether dopamine agonist treatment alone, or in early combination with levodopa, might institute a better long- term treatment in Parkinson's disease than levodopa alone. Indeed, early combination of levodopa with bromocriptine, pergolide or lisuride has indicated that this kind of treatment results in better management of Parkinson's disease with fewer fluctuations in disability, especially end- of-dose disturbances and dyskinesias, than treatment with levodopa alone. Furthermore, similar results were obtained by using lisuride in combination with selegiline and levodopa. Thus, it appears advisable to initiate the dopaminergic treatment in early Parkinson's disease by using a combination of selegiline, levodopa and a dopamine agonist. There are many ways of building up this kind of treatment. Instead of levodopa, it is possible to use initially a dopamine agonist and to add selegiline and levodopa when the therapeutic response becomes insufficient. Another alternative would be to start with selegiline alone, then to add a dopamine agonist and, finally, levodopa when clinically indicated.

L9 ANSWER 220 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1993:51662 TOXCENTER
DOCUMENT NUMBER: PubMed ID: 8101417
TITLE: Strategies in the treatment of early Parkinson's disease
AUTHOR(S): Rinne U K
CORPORATE SOURCE: Department of Neurology, University of Turku Finland
SOURCE: Acta neurologica Scandinavica. Supplementum, (1993
) Vol. 146, pp. 50-3. Ref: 26.
Journal code: 0370337. ISSN: 0065-1427.
COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
FILE SEGMENT: MEDLINE
OTHER SOURCE: MEDLINE 1993325359
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 31 Jul 2007

AB Over recent years I have been studying whether dopamine agonist treatment alone, or in early combination with levodopa, might institute a better long-term treatment in Parkinson's disease than levodopa alone. Indeed, early combination of levodopa with bromocriptine, pergolide or lisuride has indicated that this kind of treatment results in better management of Parkinson's disease with fewer fluctuations in disability, especially end-of-dose disturbances and dyskinesias, than treatment with levodopa alone. Furthermore, similar results were obtained by using lisuride in combination with selegiline and levodopa. Thus, it appears advisable to initiate the dopaminergic treatment in early Parkinson's disease by using a combination of selegiline, levodopa and a dopamine agonist. There are many ways of building up this kind of treatment. Instead of levodopa, it is possible to use initially a dopamine agonist and to add selegiline and levodopa when the therapeutic response becomes insufficient. Another alternative would be to start with selegiline alone, then to add a dopamine agonist and, finally, levodopa when clinically indicated.

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ACCESSION NUMBER: 1994138642 EMBASE
TITLE: Adrenal medullary transplants in Parkinson's disease.
AUTHOR: Clarke, H. (correspondence); Bhavani-Shankar, K.; Daisley, H.
CORPORATE SOURCE: Queen Elizabeth Hospital, Bridgetown, Barbados.
SOURCE: African Journal of Neurological Sciences, (1993)
Vol. 12, No. 2, pp. 21-23.

ISSN: 1015-8618 CODEN: AJNSDH
COUNTRY: Kenya
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 8 Jun 1994
Last Updated on STN: 8 Jun 1994

AB Parkinson's disease is a major neurodegenerative disorder, traditionally viewed as a disorder of aging, developing in increasing numbers of patients in their 30s, 40s and 50s. The current treatment of parkinson's disease consists of monoamine oxidase B inhibitors (deprenyl), dopamine agonists (bromocriptine mesylate, pergolide mesylate), carbidopa-levodopa (Sinemet), amantadine hydrochloride and anticholinergic agents used, singly or in combination. The medical treatment is satisfactory early in the disease. However, after several years, medical treatment is unsatisfactory and several patients become disabled. Adrenal transplantation surgery may offer a hope to these patients.

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ACCESSION NUMBER: 1993:32312 BIOSIS
DOCUMENT NUMBER: PREV199395020512
TITLE: Sensitive specific radioimmunoassay for quantifying
pergolide in plasma.
AUTHOR(S): Bowsheer, Ronald R. [Reprint author]; Apathy, John M.
[Reprint author]; Compton, Joyce A. [Reprint author];
Wolen, Robert L. [Reprint author]; Carlson, Kenneth H.;
Desante, Karl A.
CORPORATE SOURCE: Dep. of Drug Disposition and Bioanalytical Res., Lilly Lab.
for Clinical Res., Eli Lilly and Co., Wishard Memorial
Hospital, 1001 West Tenth St., Indianapolis, Indiana 46202,
USA
SOURCE: Clinical Chemistry, (1992) Vol. 38, No. 10, pp.
1975-1980.
CODEN: CLCHAU. ISSN: 0009-9147.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Dec 1992
Last Updated on STN: 24 Dec 1992

AB Pergolide, a synthetic ergoline with potent dopaminergic activity, is used to treat Parkinson disease. The low plasma concentrations of pergolide achieved during therapy complicate the development of a method for its analysis. Because radioimmunoassay successfully measures other structurally related ergolines in physiological fluids, we undertook the development of a radioimmunoassay of pergolide. The detection limit of the radioimmunoassay is 21 ng/L with an optimal working range from 100 to 1000 ng/L. We maximized assay specificity by using a monoclonal antibody that displayed low cross-reactivity with pergolide sulfoxide, a major metabolite found in animals. The radioimmunoassay has performed acceptably for gt 2 years during toxicology studies with rats and rhesus monkeys and in clinical studies involving patients with Parkinson disease. We consider the radioimmunoassay a valid method for quantifying therapeutic concentrations of pergolide in plasma.

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ACCESSION NUMBER: 1992289653 EMBASE
TITLE: [A new dopamine receptor antagonist: Pergolide

(permax®)].
 PERGOLIDE (PERMAX®). EEN NIEUWE
 DOPAMINERECEPTORAGONIST.

AUTHOR: Wolters, E.C., Dr. (correspondence); Kuiper, M.A.
 CORPORATE SOURCE: Afdeling Neurologie, Academisch Ziekenhuis, Vrije
 Universiteit, De Boelelaan 1117, 1081 HV Amsterdam,
 Netherlands.

SOURCE: Pharmaceutisch Weekblad, (1992) Vol. 127, No. 36,
 pp. 918-920.
 ISSN: 0031-6911 CODEN: PHWEAW

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; (Short Survey)

FILE SEGMENT: 037 Drug Literature Index
 038 Adverse Reactions Titles
 008 Neurology and Neurosurgery

LANGUAGE: Dutch; Flemish

SUMMARY LANGUAGE: Dutch; Flemish; English

ENTRY DATE: Entered STN: 25 Oct 1992
 Last Updated on STN: 25 Oct 1992

AB In July 1991 pergolide (Permax®) was registered as a drug in
 the treatment of Parkinson's disease. Because pergolide
 , in contrast to other dopamine agonists, has an obviously agonistic
 effect on the differentiated D(1) and D(2) dopamine receptors, the
 introduction of this drug the Netherlands should be accompanied by
 background information, in which we include the clinical experience which
 is already available. With the introduction of pergolide, a
 drug has become available which provides a useful alternative, particularly
 for the already maximally treated patients with Parkinson's
 disease. Because pergolide is the first dopamine agonist to be
 taken orally which may be used in monotherapy, it may also be used in
 initial treatment.

L9 ANSWER 224 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1992:3328 TOXCENTER

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DOCUMENT NUMBER: 30-10629

TITLE: Pergolide (Permax), a new dopamine receptor agonist

AUTHOR(S): Wolters, E. C.; Kuiper, M. A.

CORPORATE SOURCE: Afdeling Neurol., Acad. Ziekenhuis, Vrije Univ., De
 Boelelaan 1117, 1081 HV Amsterdam, Netherlands

SOURCE: Pharmaceutisch Weekblad (Netherlands), (Sep 4 1992
) Vol. 127, pp. 918-920. 18 Refs.
 CODEN: PHWEAW. ISSN: 0031-6911.

DOCUMENT TYPE: Journal

FILE SEGMENT: IPA

OTHER SOURCE: IPA 92:13000

LANGUAGE: German

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 16 Nov 2001
 Last Updated on STN: 16 Nov 2001

AB An overview of pergolide mesylate (Permax) is presented,
 including in vitro and in vivo pharmacology, side effects, and the drug's
 usefulness as the first dopamine agonist to be effective when taken orally
 for the treatment of Parkinson disease.
 Lisa Webster

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 STN DUPLICATE 174

ACCESSION NUMBER: 1992:458838 BIOSIS

DOCUMENT NUMBER: PREV199294100238; BA94:100238

TITLE: GENERAL PHARMACOLOGY OF PERGOLIDE IN ANIMALS 2ND
 COMMUNICATION GASTROINTESTINAL RENAL AND MISCELLANEOUS

STUDIES.
AUTHOR(S): WILLIAMS P D [Reprint author]; BENDELE A; DELDAR A; MCGARTH
J; SHETLER T; OWEN N
CORPORATE SOURCE: N MIDDLETOWN RD, PEARL RIVER, NY 10965, USA
SOURCE: Arzneimittel-Forschung, (1992) Vol. 42, No. 7,
pp. 891-895.
CODEN: ARZNAD. ISSN: 0004-4172.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 7 Oct 1992
Last Updated on STN: 8 Oct 1992

AB Pergolide mesylate ((8 β)-8-[(methylthio)methyl]-6-propylergoline monomethanesulfonate, LY 127809, CAS 66104-23-2) is a novel and potent dopamine agonist marketed for treating the symptoms of Parkinson's disease. The potential secondary pharmacological effects of this agent on the gastrointestinal and renal systems, as well as effects on local anesthesia, hemolysis, platelet aggregation, circulating blood glucose, primary antibody production, and the acute inflammatory response were examined. Pergolide exhibited significant pharmacological effects in gastrointestinal, renal and anti-inflammatory tests at high oral doses. Pergolide was essentially inactive in blood hemolysis, platelet aggregation, primary antibody production and local anesthesia testing. In summary, these studies confirm the pharmacological selectivity of pergolide, and indicate a low potential for secondary pharmacological side effects upon the functions tested at clinically relevant doses.

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ACCESSION NUMBER: 1992:372681 BIOSIS
DOCUMENT NUMBER: PREV199294054731; BA94:54731
TITLE: GENERAL PHARMACOLOGY OF PERGOLIDE IN ANIMALS 1ST
COMMUNICATION CARDIOVASCULAR RESPIRATORY AND AUTONOMIC
NERVOUS SYSTEM STUDIES.
AUTHOR(S): WILLIAMS P [Reprint author]; COLBERT W; TURK J; OWEN N
CORPORATE SOURCE: N MIDDLETOWN ROAD, PEARL RIVER, NEW YORK 10965, USA
SOURCE: Arzneimittel-Forschung, (1992) Vol. 42, No. 5,
pp. 599-607.
CODEN: ARZNAD. ISSN: 0004-4172.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 9 Aug 1992
Last Updated on STN: 9 Aug 1992

AB Pergolide mesylate ((8 β)-8-[(methylthio)methyl]-6-propylergoline monomethanesulfonate, LY 127 809, CAS 66104-23-2) is a novel and potent dopamine agonist marketed for treating the symptoms of Parkinson's disease. The potential secondary pharmacological effects of this agent on the cardiovascular, respiratory, and the autonomic nervous systems were examined. Pergolide exhibited significant pharmacological effects in cardiovascular and autonomic tests at high oral or intravenous doses. The reference dopamine agonist, bromocriptine, exhibited effects qualitatively similar to, but at doses generally higher than, pergolide, in parallel with its lower therapeutic potency relative to pergolide. In summary, these studies confirm the pharmacological selectivity of pergolide at low doses, and indicate the potential for secondary pharmacological side effects upon cardiovascular function at significant multiplies of the clinical dose.

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DUPLICATE 176

ACCESSION NUMBER: 1992:371220 BIOSIS
DOCUMENT NUMBER: PREV199294053270; BA94:53270
TITLE: DOPAMINE AGONIST TREATMENT OF FLUCTUATING PARKINSONISM D-2
CONTROLLED-RELEASE MK-458 VS COMBINED D-1 AND D-2
PERGOLIDE.
AUTHOR(S): AHLISKOG J E [Reprint author]; MUENTER M D; BAILEY P A;
STEVENS P M
CORPORATE SOURCE: DEP NEUROL, MAYO CLIN, 200 FIRST ST SW, ROCHESTER, MINN
55905, USA
SOURCE: Archives of Neurology, (1992) Vol. 49, No. 5, pp.
560-568.
CODEN: ARNEAS. ISSN: 0003-9942.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 9 Aug 1992
Last Updated on STN: 1 Oct 1992

AB Adjunctive treatment with the very potent and selective dopamine D-2
agonist MK-458 (controlled-release formulation) improved the control of
parkinsonism in patients with fluctuating responses to levodopa
therapy (with carbidopa). We subsequently switched patients to adjunctive
treatment with pergolide, a less potent D-2 agonist.
Pergolide therapy controlled parkinsonism more
effectively than controlled-release MK-458. Unlike MK-458,
pergolide meslyate also has D-1 agonist properties, apparently
accounting for its greater antiparkinsonism efficacy.
Adjunctive treatment with controlled-release MK-458 elicited less
choreiform dyskinesias than either pergolide adjunctive therapy
or therapy with carbidopa-levodopa alone; this finding suggests that D-1
receptor stimulation contributes to the elicitation of medication-induced
chorea. The highest doses of controlled-release MK-458 resulted in
paradoxical freezing of gait in almost one third of patients. This
finding suggests that gait freezing, common in untreated
parkinsonism, can also be elicited by excessive D-2 stimulation.

L9 ANSWER 228 OF 331 MEDLINE on STN DUPLICATE 177
ACCESSION NUMBER: 1992261536 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1350053
TITLE: An integrated approach to patient management in Parkinson's
disease.
AUTHOR: Lieberman A
CORPORATE SOURCE: Movement Disorders Department, Barrow Neurological
Institute, St. Josephs Medical Center, Phoenix, Arizona.
SOURCE: Neurologic clinics, (1992 May) Vol. 10, No. 2,
pp. 553-65. Ref: 35
Journal code: 8219232. ISSN: 0733-8619.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 26 Jun 1992
Last Updated on STN: 6 Feb 1995
Entered Medline: 17 Jun 1992

AB New concepts about the pathogenesis and pathophysiology of
Parkinson's disease have emerged. For these concepts to be
useful, they must be understood, and for them to be applied, the
psychology of the patient and the patient's family must be understood.
The initial consultation is crucial in establishing a successful
relationship between a patient, family, and physician. This consultation

is analyzed and ways of avoiding errors and misconceptions delineated. Emphasis is placed on imaginative questioning using the format of the ADL portion of the UPDRS in establishing the diagnosis and following treatment. The rationale for starting treatment with selegiline at this time is discussed in the context of the role that increased MAO-B activity plays in the progression of Parkinson's disease. After making the diagnosis and starting treatment with selegiline, deciding when to start levodopa is the next crucial decision. Often as important as deciding when to start levodopa is overcoming the resistance of the patient to accept this treatment. The next crucial decision occurs after the patient develops response fluctuations on levodopa. A format for assessing the fluctuations is presented, and the merits of different treatments, including selegiline, dopamine agonists (bromocriptine and pergolide), and sustained-release or controlled-release levodopa preparations (Sinemet CR), discussed. The management of patients with depression, sleep problems, and advanced disease including postural instability and mental changes are reviewed.

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ACCESSION NUMBER: 1992365301 EMBASE
 TITLE: Recent therapeutic advances in geriatric neurology.
 AUTHOR: Kuzuhara, S. (correspondence)
 CORPORATE SOURCE: Department of Neurology, Mie University School of Medicine, Tsu-shi 514, Japan.
 SOURCE: Japanese Journal of Geriatrics, (1992) Vol. 29, No. 7-8, pp. 531-539.
 ISSN: 0300-9173 CODEN: NIRZAL
 COUNTRY: Japan
 DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
 FILE SEGMENT: 020 Gerontology and Geriatrics
 030 Clinical and Experimental Pharmacology
 032 Psychiatry
 037 Drug Literature Index
 008 Neurology and Neurosurgery
 LANGUAGE: Japanese
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 10 Jan 1993
 Last Updated on STN: 10 Jan 1993

AB Marked advances in the treatment of neurological disorders which affect the elderly have been established in recent years. Cerebrovascular disorders including stroke and vascular dementia are still among the most frequent diseases in the Japanese elderly. For treatment of hypertensive patients with or without a history of stroke, slight decrease of blood pressure (BP) is recommended since recent PET studies have revealed that an excessive drop of BP markedly decreased cerebral blood flow. Furthermore, 24-hour-monitoring of BP revealed that physiological fluctuation of BP consisting of high daytime BP and low nocturnal BP disappears in hypertensive patients with vascular dementia and those with non-symptomatic vascular lesions on MRI. Recommendable BP levels for the hypertensive elderly must be established. The efficacy of both aspirin and ticlopidine for prevention of stroke has been established. Recent multi-centric trials have revealed that ticlopidine is more effective in preventing stroke but has more dangerous adverse effects than aspirin. Aspirin is reported to improve both the intellectual scale and cerebral blood flow in vascular dementia. In Parkinson's disease (PD), L-DOPA therapy, usually in combination with a dopa decarboxylase inhibitor, is common. Other dopaminergic drugs including bromocriptine, lisuride and pergolide are used clinically or are being studied. Recently selective monoamine oxidase (MAO) B inhibitors have been used in order to slow clinical progression of the disease, in addition to an attempt to increase the potential of dopamine through inhibition of MAO.

Neural transplants to the striatum of PD were first applied using autografts of the adrenal medulla in 1985, but resulted in transient or only slight improvements. In 1990, Swedish researchers reported that grafts of fetal dopamine neurons survived and improved motor function in PD. Fetal neuronal grafts seem to be promising in the treatment of PD though both biological and medicoethical matters must be solved. Although several trials of treatment of Alzheimer type dementia (ATD) have been carried out, with anti-cholinesterase agents such as physostigmine and tetrahydroaminoacridine or with other neurotransmitters, satisfactory results have not yet been obtained. Recent studies linked familial Alzheimer's disease and deposition of β -protein with the 21 chromosome. Gene biology may provide new ideas for the treatment of ATD. Several other new therapeutic methods for the treatment of neurological disorders including botulinus toxin for involuntary movements in the face and neck, immunotherapy for Lewis-Sumner syndrome, and aciclovir for herpes simplex encephalitis were described.

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ACCESSION NUMBER: 1992:260512 BIOSIS
DOCUMENT NUMBER: PREV199293136837; BA93:136837
TITLE: CHRONIC DIETARY PERGOLIDE PRESERVES NIGROSTRIATAL NEURONAL INTEGRITY IN AGED FISCHER-344 RATS.
AUTHOR(S): FELTEN D L [Reprint author]; FELTEN S Y; FULLER R W; ROMANO T D; SMALSTIG E B; WONG D T; CLEMENS J A
CORPORATE SOURCE: DEP NEUROBIOL ANATOMY, BOX 603, UNIV ROCHESTER SCH MED, 601 ELMWOOD AVE, ROCHESTER, NY 14642, USA
SOURCE: Neurobiology of Aging, (1992) Vol. 13, No. 2, pp. 339-351.
CODEN: NEAGDO. ISSN: 0197-4580.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 23 May 1992
Last Updated on STN: 23 May 1992

AB Pergolide, a potent D2 presynaptic agonist with postsynaptic D2 agonist activity and some D1 agonist activity was administered in the diet (0.5 mg/kg/day) of male Fischer 344 rats from age 3 to age 26 months. We hypothesized that the potent D2 presynaptic activity would reduce the baseline release of dopamine (DA) and thereby slow the formation of toxic oxidative metabolites that lead to age-related deterioration of nigrostriatal DA neurons. Pair-fed rats served as controls. We observed age-related losses of fluorescent DA cells bodies in the substantia nigra pars compacta and of fluorescent DA terminals in the striatum; chronic pergolide administration prevented these losses. Pergolide administration also prevented the age-related diminution of DA fluorescence intensity in substantia nigra cell bodies. A large decline in 3H-DA uptake with age was partially prevented by pergolide administration. We found no age-related alteration in the concentration of DA in the striatum and pergolide did not alter this concentration. Pergolide treatment resulted in only minor alterations in striatal 3H-spiperone binding and no change in dendritic arborizations of either DA substantia nigra neurons or medium spiny striatal neurons. Pergolide administration also prevented and age-related decline in circulating FSH levels. The uptake data and quantitative morphological findings suggest that pergolide administration in the diet for 2 years exerts a protective effect on age-related deterioration of DA nigrostriatal neurons. This finding was consistent with clinical reports of a subset of patients with Parkinson's disease in whom long-term efficacy of pergolide therapy is observed.

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STN DUPLICATE 180

ACCESSION NUMBER: 1992:283211 BIOSIS
DOCUMENT NUMBER: PREV199294007861; BA94:7861
TITLE: PARKINSONISM TREATMENT PART III. UPDATE.
AUTHOR(S): COLLIER D S [Reprint author]; BERG M J; FINCHAM R W
CORPORATE SOURCE: COLLEGE PHARMACY, UNIVERSITY IOWA, IOWA CITY, IOWA 52242,
USA
SOURCE: Annals of Pharmacotherapy, (1992) Vol. 26, No. 2,
pp. 227-233.
CODEN: APHRER. ISSN: 1060-0280.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 10 Jun 1992
Last Updated on STN: 10 Jun 1992

AB Objective: The purpose of this review is to update clinicians with recent advances in the management of parkinsonism, including drug therapy, transplantation, and diet. Data sources: Pertinent articles were obtained from an English-language literature search using MEDLINE (1970-1991), Index Medicus (1987-1991), Current Contents (1990), and bibliographic reviews of review articles. Index terms included parkinsonism, selegiline, pergolide, vitamin E, and transplantation. Fifty-five articles (representing 85 percent of the complete literature search) were selected by multiple reviewers for their contribution to the stated purpose. Emphasis was placed on double-blind, placebo-controlled, and randomized studies. Data from cited articles were examined by multiple reviewers for support of their stated hypothesis and were included as background for justification of major points in this article; critical studies were abstracted in more detail. Results: New therapeutic measures have been added to the treatment of parkinsonism. Selegiline, a monoamine oxidase inhibitor type B, has shown beneficial results, especially in early stages. Pergolide, a dopamine agonist, may be an efficacious alternative to bromocriptine resistance or intolerable adverse effects. Vitamin E may have protective antioxidant properties, but very few clinical data are available. Fetal tissue transplantation needs continued research and remains very controversial. Diet modifications may maximize the results of therapy with exogenous dopamine therapy. Conclusions: Clinicians should familiarize themselves with new alternatives for the management of parkinsonism in order to be reliable consultants for both professional and lay persons.

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ACCESSION NUMBER: 1992116942 EMBASE
TITLE: Parkinson's disease: Update on pharmacologic options to slow progression and treat symptoms.
AUTHOR: Ahlskog, J.E.
SOURCE: Hospital Formulary, (1992) Vol. 27, No. 2, pp. 146-163.
ISSN: 0098-6909 CODEN: HOFOD9
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 15 May 1992
Last Updated on STN: 15 May 1992

AB Medical treatment of Parkinson's disease is becoming increasingly complex. Carbidopa/levodopa continues to be the most

efficacious medication available. Other recent evidence suggests that selegiline might slow Parkinson's disease progression. The direct-acting dopamine agonists, bromocriptine and pergolide, are often beneficial in patients with short-duration, fluctuating levodopa responses. These medications have also been advocated for initial symptomatic treatment, concurrent with the initiation of carbidopa/levodopa; however, this use is controversial. The controlled-release formulation of carbidopa/levodopa typically prolongs the levodopa response by approximately 30%, but some patients prefer the standard formulation due to its faster onset of action. The expense of using two or more of these medications is of concern to this patient population.

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ACCESSION NUMBER: 1992:83 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 29-04761
TITLE: Parkinson's disease: update on pharmacologic options to slow progression and treat symptoms
AUTHOR(S): Ahlskog, J. E.
CORPORATE SOURCE: Mayo Clin., Dept. of Neurol., 200 First St. SW, Rochester, MN 55905, USA
SOURCE: Hospital Formulary (USA), (Feb 1992) Vol. 27, pp. 146-152, 161-163. 92 Refs.
CODEN: HOFOD9. ISSN: 0098-6909.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 92:231
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB Parkinson's disease, including therapy for early and late disease, results of clinical studies, drug interactions, adverse effects, and costs of medications, is discussed. Drug therapy with such agents as selegiline, alpha-tocopherol, levodopa, bromocriptine, pergolide, carbidopa/levodopa (Sinemet CR), and adjunctive therapy with baclofen (Lioresal) and antidepressants are included.
Kate Gibbons

L9 ANSWER 234 OF 331 MEDLINE on STN DUPLICATE 182

ACCESSION NUMBER: 1992195439 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1347909
TITLE: Initiating treatment of Parkinson's disease.
AUTHOR: Koller W C
CORPORATE SOURCE: Department of Neurology, University of Kansas Medical Center, Kansas City, KS 66103.
SOURCE: Neurology, (1992 Jan) Vol. 42, No. 1 Suppl 1, pp. 33-8; discussion 57-60. Ref: 67
Journal code: 0401060. ISSN: 0028-3878.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 9 May 1992
Last Updated on STN: 6 Feb 1995
Entered Medline: 20 Apr 1992

AB Treatment of Parkinson's disease (PD) can be divided into two categories: symptomatic therapy (restoring dopamine levels toward normal and reversing functional disability) and preventive therapy (interfering with the pathophysiologic mechanism of PD to prevent or decrease the rate

of progression of the disease). Regarding symptomatic treatment, although anticholinergic preparations generally are considered effective for the symptoms of tremor and rigidity without altering bradykinesia, their effectiveness is limited and adverse reactions are common; their role should be restricted to use as adjuvants to levodopa therapy. Amantadine has been shown to be as effective as anticholinergics, but it lacks long-term efficacy. Dopamine agonists--bromocriptine, pergolide mesylate and lisuride in Europe--are not as effective as levodopa and therefore rarely are used as initial therapy; their proposed role, too, is as adjuvants to levodopa therapy. Levodopa is the most effective drug presently available for the treatment of PD; its introduction is accompanied by rapid and dramatic reduction of symptoms and signs. Initial adverse reactions are not usually a major problem; and although there is speculation that initiation of therapy should be delayed because of possible long-term complications, clinically distinguishing these from problems related to disease progression itself is difficult. The possibility that nigral cell death is mediated by oxidative mechanisms provides the basis for considering antioxidant therapy as protective treatment; selegiline, an antioxidant, has been found to delay the need for symptomatic therapy. It is suggested that initial treatment of Parkinson's disease begin with both preventive therapy with selegiline and symptomatic treatment with the sustained-release preparation of levodopa, which may be associated with fewer long-term complications.

L9 ANSWER 235 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 183
 ACCESSION NUMBER: 1994:400043 CAPLUS
 DOCUMENT NUMBER: 121:43
 ORIGINAL REFERENCE NO.: 121:3a,6a
 TITLE: Neuroprotection
 AUTHOR(S): Clemens, James A.; Fuller, Ray W.; Felten, Suzanne Y.; Felten, David L.
 CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
 SOURCE: Curr. Trends Treat. Parkinson's Dis., [Proc. Symp.] (1992), Meeting Date 1991, 19-27. Editor(s): Agid, Yves. Libbey: London, UK.
 CODEN: 59YCAG
 DOCUMENT TYPE: Conference; General Review
 LANGUAGE: English
 AB A review with 12 refs. Pergolide, a potent dopamine agonist with activity in both D1 and D2 dopamine receptors, when fed in the diet to Fischer 344 rats produced a long-lasting decrease in dopamine turnover and significantly reduced the aged-related loss of dopamine neurons. The authors observed an age-related loss of fluorescent dopamine cell bodies in the substantia nigra pars compacta and of fluorescent dopamine terminals in the striatum; chronic pergolide treatment prevented these losses. The large decline in 3H-dopamine reuptake with age was partially prevented by pergolide administration. Beneficial effects on the hypothalamo-pituitary-gonadal axis were also observed (-)Deprenyl, a monoamine oxidase inhibitor, is another agent that appears to have neuroprotective effects. It was reported to prolong the life span in rats and slow the progression of Parkinson's disease. Interestingly, a recent study reported that (-)deprenyl increased striatal levels of superoxide dismutase and catalase, two enzymes that are important for the cell's defense against superoxide and hydrogen peroxide. In conclusion, toxic products formed from dopamine may lead to an accelerated degeneration of dopamine neurons, and agents that reduce dopamine availability, prevent its oxidation or prevent toxicity of oxygen radicals derived from its oxidation may be useful in preserving the integrity of the nigrostriatal dopaminergic system.
 OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD

(2 CITINGS)

L9 ANSWER 236 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1992:440228 CAPLUS

DOCUMENT NUMBER: 117:40228

ORIGINAL REFERENCE NO.: 117:6935a,6938a

TITLE: Motor responses to dopamine D1 and D2 agonists in the reserpine-treated mouse are affected differentially by the NMDA receptor antagonist MK 801

AUTHOR(S): Goodwin, P.; Starr, B. S.; Starr, M. S.

CORPORATE SOURCE: Dep. Pharmacol., Sch. Pharm., London, UK

SOURCE: Journal of Neural Transmission: Parkinson's Disease and Dementia Section (1992), 4(1), 15-26
CODEN: JNPSEJ; ISSN: 0936-3076

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The akinesia induced by reserpine in mice was effectively reversed by the dopamine D1 receptor agonists SKF 38393 (5-30 mg/kg i.p.) and CY 208-243 (1-5 mg/kg IP), and by the mixed D1/D2 agonist pergolide (5 mg/kg SC), but less well by the D2 agonists lisuride, PHNO, LY 171555 and RU 24213 (each at 5 mg/kg SC) and not at all by the NMDA receptor antagonist MK 801 (0.1-10 mg/kg IP). MK 801 potentiated D1-dependent locomotion, but always suppressed rearing and grooming. D2-dependent locomotion was inhibited by MK 801. The D2 agonist RU 24213 was antagonized by as little as 6.25 µg/kg MK 801, while PHNO and LY 171555 were antagonized by 0.1 mg/kg MK 801. Lisuride was not inhibited by up to 1.6 mg/kg MK 801. Importantly, all animals showed signs of incapacitation with MK 801 in certain elements of their behavior, most notably ataxia and hind limb abduction. Thus, while NMDA receptor blockade can facilitate the restoration of movement by dopamine D1 (though not D2) agonists in monoamine-depleted mice, the fluency of the motor response is adversely affected. The results are discussed in relation to the treatment of Parkinson's disease.

OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)

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ACCESSION NUMBER: 1991242941 EMBASE

TITLE: Pergolide: A dopamine agonist at both D(1) and D'2 receptors.

AUTHOR: Fuller, R.W.; Clemens, J.A.

CORPORATE SOURCE: Lilly Research Laboratories, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285, United States.

SOURCE: Life Sciences, (1991) Vol. 49, No. 13, pp. 925-930.

ISSN: 0024-3205 CODEN: LIFSAK

COUNTRY: United States

DOCUMENT TYPE: Journal; (Short Survey)

FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 16 Dec 1991

Last Updated on STN: 16 Dec 1991

AB Pergolide is a potent, direct-acting dopamine agonist used in treating Parkinson's disease. It is an agonist found recently to have high affinity fo D(3) receptors. The affinity of pergolide for D(1) receptors is lower than for D(2) receptors, and there have been some reports that it may not interact with D(1) receptors in vivo at doses used to activate D(2) receptors. A growing body of

evidence suggests that pergolide does occupy and activate D(1) receptors in vivo, although the relevance to therapeutic efficacy in Parkinson's disease needs further study.

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ACCESSION NUMBER: 1991259533 EMBASE
TITLE: Behavioral complications of drug treatment of Parkinson's disease.
AUTHOR: Cummings, J.L.
CORPORATE SOURCE: Neurobehavior Unit, West LA VAMC, 11301 Wilshire Blvd., Los Angeles, CA 90073, United States.
AUTHOR: Cummings, J., Dr. (correspondence)
CORPORATE SOURCE: Neurobehavior Unit, West LA VAMC, 11301 Wilshire Blvd., Los Angeles, CA 90073, United States.
SOURCE: Journal of the American Geriatrics Society, (1991) Vol. 39, No. 7, pp. 708-716.
ISSN: 0002-8614 CODEN: JAGSAF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 020 Gerontology and Geriatrics
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Dec 1991
Last Updated on STN: 16 Dec 1991

AB A variety of neuropharmacologic agents, including anticholinergic drugs, amantadine hydrochloride, levodopa, selegiline, bromocriptine, and pergolide, are now available for the treatment of Parkinson's disease. Of patients treated with dopaminergic agents, 30% develop visual hallucinations, 10% exhibit delusions, 10% have euphoria, 1% have mania, 10% to 15% experience increased anxiety, 15% have confusional periods, and a few exhibit altered sexual behavior. Anticholinergic drugs have a greater tendency to produce confusional states than dopaminergic compounds. Elderly patients and those with underlying dementia are most likely to have untoward side effects with anti-parkinsonism treatment. Dosage reduction is the optimum management strategy, although anti-psychotic agents may be necessary in patients with delusions, and lithium may help control drug-induced mania. Dopaminergic agents share the property of stimulation of D2 dopamine receptors, and this action may play an essential role in mediating their neuropsychiatric effects.

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ACCESSION NUMBER: 1991:2681 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 29-08653
TITLE: Drug therapy for Parkinson's disease
AUTHOR(S): Shimp, L. A.
SOURCE: Journal Michigan Pharmacist, (Dec 1991) Vol. 29, pp. 448-451, 453.
ISSN: 0026-2404.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 91:11025
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB The pathologic brain changes that cause the signs and symptoms of

Parkinson's disease and the use and side effects of anticholinergics, levodopa-carbidopa, amantadine, bromocriptine, pergolide, and selegiline are discussed. This article qualifies for one hour of U.S. CE credit by the ACPE.
Anne L. Morisseau

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ACCESSION NUMBER: 1991:457609 BIOSIS
DOCUMENT NUMBER: PREV199192102389; BA92:102389
TITLE: REDUCED D2 DOPAMINE AND MUSCARINIC CHOLINERGIC RECEPTOR
DENSITIES IN CAUDATE SPECIMENS FROM FLUCTUATING
PARKINSONIAN PATIENTS.
AUTHOR(S): AHLSSKOG J E [Reprint author]; RICHELSON E; NELSON A; KELLY
P J; OKAZAKI H; TYCE G M; VAN HEERDEN J A; STODDARD S L;
CARMICHAEL S W
CORPORATE SOURCE: DEP NEUROL, MAYO CLIN, ROCHESTER, MINN 55905, USA
SOURCE: Annals of Neurology, (1991) Vol. 30, No. 2, pp.
185-191.
CODEN: ANNED3. ISSN: 0364-5134.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 11 Oct 1991
Last Updated on STN: 8 Jan 1992

AB Binding of spiperone and 3-quinuclidinyl benzilate (QNB), both labeled with hydrogen 3 (3H), were measured in caudate tissue obtained from 8 living parkinsonian patients at the time of cerebral transplantation. This was a clinically homogeneous group of patients: All remained predominantly responsive to levodopa, although with marked disability secondary to clinical fluctuations (short-duration responses) and medication-induced dyskinesias; all were receiving substantial doses of levodopa and 6 of the 8 patients were additionally receiving bromocriptine or pergolide. Binding densities of dopamine D2 receptors, as measured by [3H]spiperone binding, were reduced in this group of patients, compared to caudate specimens from autopsy control subjects. This finding may reflect medication-induced receptor downregulation. Parallel changes occurred with muscarinic cholinergic receptors; [3H]QNB binding was significantly reduced, compared to autopsy control values. This reduction of muscarinic receptors might be due to loss of nigrostriatal terminals that are known to contain muscarinic receptors. Alternatively, muscarinic receptors may have been downregulated by increased corticostriatal glutamatergic input to cholinergic cells, inferred to be present based on the prominent levodopa-induced dyskinesias. Finally, receptor deficits could have also been a reflection of more widespread degenerative cerebral disease, although levodopa-refractory symptoms were generally not pronounced in these patients.

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ACCESSION NUMBER: 1992:8577 BIOSIS
DOCUMENT NUMBER: PREV199293008577; BA93:8577
TITLE: ANTI-INFLAMMATORY ACTIVITY OF PERGOLIDE A DOPAMINE RECEPTOR
AGONIST.
AUTHOR(S): BENDELE A M [Reprint author]; SPAETHE S M; BENSLAY D N;
BRYANT H U
CORPORATE SOURCE: ELI LILLY CO, INDIANAPOLIS, INDIANA 46285, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (1991) Vol. 259, No. 1, pp. 169-175.
CODEN: JPETAB. ISSN: 0022-3565.
DOCUMENT TYPE: Article

FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 6 Mar 1992

AB Pergolide, a dopamine agonist effective in the treatment of Parkinson's disease, has been shown to have anti-inflammatory activity in the carrageenan paw edema assay in rats at p.o. doses greater than or equal to 0.3 mg/kg. Studies were done to investigate the mechanism of action and to determine the pharmacologic significance of this finding. Because pergolide elevates circulating glucocorticoids, the effect of pergolide on carrageenan-induced paw swelling was assessed in adrenalectomized rats. Pergolide retained its anti-inflammatory activity in adrenalectomized carrageenan-injected rats, thus eliminating corticosterone induction as a possible mechanism of action. Pergolide treatment also did not decrease thromboxane B₂, prostaglandin E₂ or leukotriene B₄ production, ruling out direct effects on arachidonic acid inflammatory mediators. Interactions with the autonomic nervous system were suggested, in that an alpha adrenergic alpha agonist (clonidine) mimicked the activity of pergolide in the carrageenan assay, and an alpha adrenergic antagonist (phenoxybenzamine) blocked the anti-inflammatory activity of pergolide in this assay. Dopamine receptor antagonists (haloperidol or sulpiride) partially inhibited the effect of pergolide in the carrageenan model. However, the peripherally restricted dopamine antagonist, domperidone, was ineffective, suggesting that a central dopamine receptor was involved in the effect. Experiments in chronic inflammation models such as lipoidal-amine induced arthritis in rats and picryl chloride-induced delayed type hypersensitivity in mice also revealed an anti-inflammatory effect of pergolide. Activity in the carrageenan system and the lipoidalamine model demonstrated that the anti-inflammatory effects of pergolide were separable from potential immunosuppressive effects. Multiple dose studies indicated that tolerance might develop to the anti-inflammatory effect of pergolide. Results of these studies indicated that treatment of rats with pergolide resulted in nonimmunologically mediated anti-inflammatory activity that was not a result of corticosterone induction or decreased production of arachidonic acid metabolites. Rather, the antiinflammatory effect seemed to be dependent upon effects on the sympathetic nervous system.

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ACCESSION NUMBER: 1991:253587 BIOSIS
DOCUMENT NUMBER: PREV199191134142; BA91:134142
TITLE: COMPARISON OF COMBINATION PERGOLIDE AND L DOPA TO L DOPA
ALONE AFTER 63 MONTHS OF TREATMENT.
AUTHOR(S): ZIMMERMAN T [Reprint author]; SAGE J I
CORPORATE SOURCE: DEP NEUROL, UMDNJ-ROBERT WOOD JOHNSON MED SCH, CN19, NEW
BRUNSWICK, NJ 08903, USA
SOURCE: Clinical Neuropharmacology, (1991) Vol. 14, No.
2, pp. 165-169.
CODEN: CLNEDB. ISSN: 0362-5664.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 25 May 1991
Last Updated on STN: 25 May 1991

AB We retrospectively compared the clinical state of 14 patients with Parkinson's disease who took pergolide continuously for 63 ± 17 months (Group I) to that of 12 similar patients who started pergolide and then stopped it after 60 ± 5 days (Group II). Disability measured during the "on" state did not worsen during the

observations period in Group I patients, whereas disability in Group II showed significant deterioration. There were no significant differences in the progression of motor fluctuations between the two groups. Combination treatment with pergolide and levodopa is effective long-term symptomatic therapy for advanced Parkinson's disease and deserves more rigorous study to determine whether or not it also retards progression of Parkinson's disease.

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ACCESSION NUMBER: 1991300981 EMBASE
 TITLE: Antiparkinsonian dopamine agonists: A review of the pharmacokinetics and neuropharmacology in animals and humans. Review article.
 AUTHOR: Wachtel, H.
 CORPORATE SOURCE: Department of Neuropsychopharmacology, Schering AG, Mullerstrasse 170-178, W-1000 Berlin 65, Germany.
 SOURCE: Journal of Neural Transmission - Parkinson's Disease and Dementia Section, (1991) Vol. 3, No. 3, pp. 151-201.
 ISSN: 0936-3076 CODEN: JNPSEJ
 COUNTRY: Austria
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 020 Gerontology and Geriatrics
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 008 Neurology and Neurosurgery
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 18 Dec 1991
 Last Updated on STN: 18 Dec 1991

AB With the intention of compensating for the deficit of endogenous dopamine (DA) in the basal ganglia of Parkinsonian patients by substitution with agents which directly stimulate central DA receptors, synthetic DA agonists have been introduced almost 20 years ago for the symptomatic treatment of Parkinson's disease. The original expectation that DA agonists would be able to completely restore extrapyramidal motor function in Parkinsonian patients has turned out as too mechanistic and simplistic. However, undoubtedly DA agonists have improved therapeutic possibilities in Parkinson's disease. Thus, clinical evidence from controlled chronic studies in patients indicates that the therapeutic results following the early application of DA agonists in combination with L-DOPA on a long-term base are superior to the respective monotherapy. However, none of the DA agonists currently employed for antiparkinsonian treatment i.e. apomorphine and the ergoline derivatives bromocriptine, lisuride and pergolide, is optimal with respect to pharmacokinetic properties (poor oral bioavailability with considerable intra- and interindividual variation) or pharmacological profiles (low selectivity for DA receptors in case of the ergot agonists). The pathophysiology underlying Parkinson's disease which turned out more complex than initially expected might provide another explanation for the limited therapeutic potential of DA agonists. Therefore, apart from summarizing the pharmacokinetics, biotransformation, neuropharmacology and neurobiochemistry of the DA agonists employed clinically, the present article also reviews physiological aspects of (a) central dopaminergic neurotransmission including the topographical distribution of DA receptor subtypes and their functional significance, (b) the intracellular processing in striatal output neurons and (c) the intraneuronal mechanisms which integrate the various neurotransmitter signals converging on the striatal output neuron to a demand-adjusted effector cell response via the cross-talk between the different second messenger systems. Based on these

considerations, potential pharmacological approaches for the development of improved antiparkinsonian drugs are outlined. There is a therapeutic demand for more selective and better bioavailable DA agonists. In particular, selective D-1 receptor agonists are highly desirable to provide a more specific probe than SKF 38 393 for clarifying the current controversy on the disparate findings in nonprimate species and monkeys or Parkinsonian patients, respectively, regarding the functional significance of D-1 receptors for the antiparkinsonian action of DA agonists or L-DOPA. The therapeutic importance of D-2 receptor activation is generally accepted; whether DA agonists combining a balanced affinity to both D-1 and D-2 receptors within one molecule (to some extent a property of apomorphine) might be superior to subtype-specific DA agonists remains to be tested clinically. Beside selective DA agonists with markedly increased absolute oral bioavailability, the following alternative approaches for the symptomatic treatment of Parkinson's disease seem worth pursuing: (a) diminution of excitatory amino acid (EAA)-mediated neurotransmission in the basal ganglia output nuclei, e.g. by EAA receptor antagonists, (b) pharmacological manipulation of the intracellular second messenger signals generated by DA, EAA's or acetylcholine in the striatal output neurons. Furthermore, preliminary experimental evidence indicates that, apart from symptomatic treatment, a preventive (neuroprotective) therapy of Parkinson's disease might be conceivable with EAA receptor antagonists.

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ACCESSION NUMBER: 1992035022 EMBASE

TITLE: New strategies in the treatment of early Parkinson's disease.

AUTHOR: Rinne, U.K. (correspondence)

CORPORATE SOURCE: Department of Neurology, University of Turku, SF-20520 Turku, Finland.

SOURCE: Acta Neurologica Scandinavica, Supplement, (1991)
Vol. 84, No. 136, pp. 95-98.
ISSN: 0065-1427 CODEN: ANSLAC

COUNTRY: Denmark

DOCUMENT TYPE: Journal; (Short Survey)

FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20 Mar 1992

Last Updated on STN: 20 Mar 1992

AB Over recent years I have been studying whether dopamine agonist treatment alone, or in early combination with levodopa, might institute a better long-term treatment in Parkinson's disease than levodopa alone. Indeed, early combination of levodopa with bromocriptine, pergolide or lisuride has indicated that this kind of treatment results in better management of Parkinson's disease with fewer fluctuations in disability, especially end-of-dose disturbances and dyskinesias, than treatment with levodopa alone. Furthermore, similar results were obtained by using lisuride in combination with selegiline and levodopa. However, during long-term treatment the changes in parkinsonian disability were equal in all treatment groups with or without selegiline. Thus, the possible efficacy of selegiline in slowing down the progression of Parkinson's disease requires further investigations. As a new treatment strategy it appears advisable to initiate the dopaminergic treatment in early Parkinson's disease by using initially selegiline and a dopamine agonist and by adding levodopa when the therapeutic response is insufficient. Another alternative would be to start with selegiline alone, then add a dopamine agonist and, finally, levodopa.

L9 ANSWER 245 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 191

ACCESSION NUMBER: 1991:253622 BIOSIS
DOCUMENT NUMBER: PREV199191134177; BA91:134177
TITLE: PERGOLIDE MESYLATE FOR REFRACTORY PARKINSON'S DISEASE FIRST
ITALIAN EXPERIENCE.
AUTHOR(S): PEZZOLI G [Reprint author]; ZECCHINELLI A; MARIANI C;
REGANATI P; SCARLATO G
CORPORATE SOURCE: VIA F SFORZA 43, MILANO
SOURCE: Clinica Terapeutica, (1991) Vol. 136, No. 1, pp.
39-45.
CODEN: CLTEA4. ISSN: 0009-9074.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ITALIAN
ENTRY DATE: Entered STN: 25 May 1991
Last Updated on STN: 16 Jul 1991

AB Sixteen parkinsonian patients, mean age 57 (range 41-71), with a mean 9 year duration of Parkinson's disease, with on-off motor fluctuations were treated with pergolide mesylate 1.6 mg/die (range 1-5) for three months. The treatment resulted in an improvement of akinesia, tremor and rigidity, of the severity of phase off and of the duration of time on. No significant improvements were obtained in the severity of dyskinesia. Three patients considered the treatment excellent and capable of restoring their working abilities. The drug was generally well tolerated. Pergolide was discontinued because of orthostatic hypotension in two patients and because of hallucinations in one patient. We consider these results a favorable progress in the treatment of Parkinson's disease.

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ACCESSION NUMBER: 1991:140709 BIOSIS
DOCUMENT NUMBER: PREV199191077249; BA91:77249
TITLE: EARLY COMBINATION OF SELEGILINE AND LOW-DOSE L DOPA AS
INITIAL SYMPTOMATIC THERAPY IN PARKINSON'S DISEASE
EXPERIENCE IN 26 PATIENTS RECEIVING COMBINED THERAPY FOR 26 MONTHS.
AUTHOR(S): ELIZAN T S [Reprint author]; MOROS D A; YAHR M D
CORPORATE SOURCE: DEP NEUROLOGY, BOX 1137, MOUNT SINAI MED CENTER, 1 GUSTAVE
L LEVY PL, NEW YORK NY 10029, USA
SOURCE: Archives of Neurology, (1991) Vol. 48, No. 1, pp.
31-34.
CODEN: ARNEAS. ISSN: 0003-9942.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 14 Mar 1991
Last Updated on STN: 22 May 1991

AB Thirty-eight patients newly diagnosed as having Parkinson's disease (mean age, 57.3 years; mean Parkinson's disease duration, 2.7 years) in the earlier phase of the disease (mean Hoehn/Yahr stage, 2; mean motor scores, 11.4) were given selegiline (Deprenyl), 10 mg daily, and maintained on this drug alone until significant clinical worsening warranted the addition of low-dose levodopa (Sinemet, 25/100 three to four doses per day). Five of these patients were not yet receiving additional levodopa despite some worsening of motor scores. Of the 33 patients now taking combined therapy, seven have been followed up for 6 months or less. Twenty-four (92%) of the 26 patients taking combined therapy for a mean of 26 months (8.5 to 99 months) who have had Parkinson's disease for 6 years showed a dramatic improvement in

their parkinsonism shortly after the addition of levodopa, with significant decreases in their rated motor scores, such improvement being maintained at their latest neurologic evaluation. Eighteen (75%) of these 24 patients responded to the combined selegiline/levodopa therapy with degrees of improvement equal to or greater than 50%, compared with their motor status at the start of combined therapy just before the addition of levodopa. This degree of "reversal" of parkinsonism on addition of levodopa (mean carbidopa/levodopa dose, 98/380 mg) was not observed in any of these same patients receiving selegiline alone for an average of 13.8 months. Four patients taking combined therapy developed mild, transient, abnormal involuntary movements, and end-of-dose pattern of response after more than 2 years of combined therapy (24.75 and 33.5 months, respectively). Our results on combined selegiline/levodopa therapy reemphasize the continuing dominant role of levodopa as the primary drug for the symptomatic treatment of Parkinson's disease. A possible synergistic role of selegiline with levodopa in the early cases is suggested by the sustained therapeutic effectiveness of even low doses of the latter for a period of 26 months, with a delay in the appearance of relatively minor side effects developing only after more than 2 years of combined therapy. At an average disease duration of 6 years, no patient has had a major functional disability. A concurrently studied control group of patients treated with low-dose levodopa alone, or one treated with a combination of low-dose levodopa and a dopamine agonist like bromocriptine or pergolide, may have clarified further the role of selegiline, but such control subjects were not available to us at this time. We suggest the early combination of a selective monoamine oxidase type B inhibitor like selegiline, and the original dopamine replacement drug, levodopa (as low-dose Sinemet), as initial symptomatic therapy in newly diagnosed cases of Parkinson's disease.

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ACCESSION NUMBER: 1991:59500 BIOSIS
DOCUMENT NUMBER: PREV199140024855; BR40:24855
TITLE: PARKINSON'S DISEASE A GUIDE FOR PATIENT AND FAMILY THIRD EDITION.
AUTHOR(S): DUVOISIN R C [Reprint author]
CORPORATE SOURCE: DEP NEUROL, UNIV MED AND DENT NJ, ROBERT WOOD JOHNSON MED SCH, NJ, USA
SOURCE: (1990) pp. XI+207P. DUVOISIN, R. C. PARKINSON'S DISEASE: A GUIDE FOR PATIENT AND FAMILY, THIRD EDITION. XI+207P. RAVEN PRESS: NEW YORK, NEW YORK, USA. ILLUS. ISBN: 0-88167-729-9 (PAPER), 0-88167-711-6 (CLOTH).
DOCUMENT TYPE: Book
FILE SEGMENT: BR
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 19 Jan 1991
Last Updated on STN: 19 Jan 1991

AB This book, in its third edition, is recommended highly to patients, their spouses, family and friends, and to practicing neurologists. It has been written by an experienced doctor who goes into great detail concerning symptoms and their variability, treatment, and useful drugs and their side effects. Drug treatments discussed include the slow-release formulations of levodopa, combination of levodopa with bromocriptine, pergolide, or selegiline, and the use of anticholinergic drugs. The surgical treatment of parkinsonism, dietary considerations, exercise, historical perspectives, and future prospects including recent discoveries, fresh insights, new technologies, young scientists entering the field, and recent progress toward identifying the underlying genetic deficit are also described. Illustrations, black-and-white photographs, and a glossary supplement this book. Also, appendices list the organizations concerned with Parkinson's disease and the trade

names, generic names, and formulations of commonly prescribed drugs.

L9 ANSWER 248 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:562529 TOXCENTER

DOCUMENT NUMBER: DART-TER-90000488

TITLE: Developmental toxicology of the dopamine agonist pergolide mesylate in CD-1 mice.

AUTHOR(S): Buelke-Sam J; Byrd R A; Johnson J A; Tizzano J P; Owen N V

CORPORATE SOURCE: Toxicol. Div., Lilly Res. Labs, Eli Lilly & Co., Greenfield, IN.

SOURCE: Teratology, (1990 May) 41 (5) 619-20.
ISSN: 0040-3709.

DOCUMENT TYPE: Abstract; (Meeting Abstract)

FILE SEGMENT: DART

LANGUAGE: English

ENTRY DATE: Entered STN: Dec 2002

Last Updated on STN: Dec 2002

AB Pergolide mesylate is a dopamine agonist used in the treatment of Parkinson's disease. A total of 180 mated female CD-1 mice (copulatory date = gestation day 0 (GD 0)) were treated orally on GD 6-15 at doses of 0, 1, 20, or 60 mg/kg/day pergolide mesylate. On GD 18, 25 females/treatment group were killed, maternal reproductive parameters were assessed and complete fetal examinations were performed. Twenty females/group were allowed to deliver litters, and offspring growth, development, and behavioral and reproductive performance were monitored. Maternal weight gain and food consumption were reduced during GD 6-11 in the 60 mg/kg group. Fetal body weights also were decreased significantly at this dose but there were no treatment-related changes in fetal viability or morphology. In the delivery segment of this study, mean offspring survival, body weights, morphological indices, and reproductive performance were not affected adversely by treatment. Onset of negative geotaxis was delayed approximately 1 day in the 20 and 60 mg/kg groups and increased auditory startle amplitude was seen in 55-day-old male offspring of the 60 mg/kg group. One-hour activity levels at 30 and 60 days of age as well as active and passive avoidance performance evaluated between 61 and 70 days of age were not affected adversely by prenatal exposure to pergolide mesylate.

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ACCESSION NUMBER: 1990048730 EMBASE

TITLE: New concepts in the treatment of Parkinson's disease.

AUTHOR: Ahlskog, J.E.; Wilkinson, J.M.

CORPORATE SOURCE: Mayo Medical School, Rochester, MN, United States.

SOURCE: American Family Physician, (1990) Vol. 41, No. 2, pp. 574-584.

ISSN: 0002-838X CODEN: AFPYAE

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 037 Drug Literature Index

038 Adverse Reactions Titles

008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 13 Dec 1991

Last Updated on STN: 13 Dec 1991

AB Carbidopa/levodopa remains the most potent drug for the treatment of Parkinson's disease. Several newer medications may help stabilize and improve such problems as fluctuating responses to the medication, drug-induced dyskinesias and refractory symptoms. Patients with fluctuating responses that do not respond to adjustments in the carbidopa/levodopa dose may benefit from the addition of a direct-acting

dopamine agonist, such as pergolide or bromocriptine. While carbidopa/levodopa and the direct-acting dopamine agonists have a proven track record as symptomatic treatment, they probably do not alter the pathologic process underlying this progressive condition. On the other hand, two studies have shown that selegiline might slow the progression of Parkinson's disease, independent of any direct effects on symptoms.

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ACCESSION NUMBER: 1990120122 EMBASE
TITLE: Pergolide. A review of its pharmacological properties and therapeutic potential in Parkinson's disease.
AUTHOR: Langtry, H.D.; Clissold, S.P.
CORPORATE SOURCE: ADIS Drug Information Services, 41 Centorian Drive, Mairangi Bay, Auckland 10, New Zealand.
SOURCE: Drugs, (1990) Vol. 39, No. 3, pp. 491-506.
ISSN: 0012-6667 CODEN: DRUGAY
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 1991
Last Updated on STN: 13 Dec 1991

AB When used to treat patients with Parkinson's disease pergolide acts at dopamine receptors in the corpus striatum to improve locomotor activity, reducing the tremor, gait disturbances, bradykinesia or akinesia and rigidity experienced by such patients. Treatment with pergolide often allows substantial reductions in concomitant levodopa dosage, and occasionally levodopa can be completely replaced by pergolide therapy in short term use. Pergolide has a long duration of action, thus reducing the wearing-off and end-of-dose phenomena frequently seen with long term levodopa therapy, suppressing fluctuations in levodopa response, and increasing total 'on' time. Despite a lack of well controlled studies comparing this drug with other dopamine agonist agents, pergolide appears to result in adverse effects and anti-Parkinson responses similar to those of bromocriptine and lisuride. Thus, pergolide would appear to be at least as useful as other dopamine agonists such as bromocriptine or lisuride for the management of patients with Parkinson's disease when administered in combination with levodopa. Future research should be directed towards establishing which patients are most likely to benefit from pergolide therapy, and clarifying the relative efficacy and safety of the anti-Parkinsonian drugs available to the clinician. If pergolide does provide clinical benefit when substituted for levodopa-adjunct drugs that are producing less than optimal control, this will be an advantage in a disease area which at present has few therapeutic options.

L9 ANSWER 251 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1990:481 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 27-12453
TITLE: New alternatives for the treatment of Parkinson's disease
AUTHOR(S): Erwin, W. G.
CORPORATE SOURCE: Philadelphia Coll. of Pharm. and Sci., Philadelphia, PA, USA

SOURCE: American Druggist (USA), (Feb 1990) Vol. 201,
pp. 62, 64, 66, 68, 70, 72.
CODEN: AMDRAG. ISSN: 0190-5279.

DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 90:1519
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB The pathophysiology, clinical symptoms and treatment of Parkinson disease are discussed. Long term complications of levodopa therapy and the use, dosage and problems associated with pergolide mesylate (Permax) and selegiline hydrochloride (Eldepryl) are described. This article qualifies for 2 hours U.S. CE credit by the ACPE.
Ellen Katz Neumann

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STN DUPLICATE 195

ACCESSION NUMBER: 1989:452228 BIOSIS
DOCUMENT NUMBER: PREV198988100500; BA88:100500
TITLE: AGONIST SUBSTITUTION IN ADVANCED PARKINSON'S DISEASE.
AUTHOR(S): GOETZ C G [Reprint author]; SHANNON K M; TANNER C M;
CARROLL V S; KLAUANS H L
CORPORATE SOURCE: DEP NEUROL SCI, RUSH PRESBYTERIAN ST LUKE'S MED CENT, 1725
W HARRISON ST, CHICAGO, ILL 60612, USA
SOURCE: Neurology, (1989) Vol. 39, No. 8, pp. 1121-1122.
CODEN: NEURAI. ISSN: 0028-3878.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 4 Oct 1989
Last Updated on STN: 6 Oct 1989

AB We studied whether Parkinson's disease patients who had lost efficacy from pergolide (PERG) could benefit if transferred to bromocriptine (BCT) therapy. Using paired t-tests, we compared motor scores at baseline (when patients were still on PERG) and after 6 months of BCT therapy in 11 patients. No significant improvement occurred in any measure on BCT therapy (mean dose 33.6 mg/day), although patients remained stable. In 6 patients on whom "on/off" data were obtained, decreased "off" time and increased "on" time without chorea occurred, but these changes were not statistically significant. The side effect profile was similar with the 2 drugs.

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ACCESSION NUMBER: 1989:2290 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 27-05702
TITLE: Pergolide mesylate
AUTHOR(S): Carrell, S. A.; Robinson, C. P.
CORPORATE SOURCE: Univ. of Oklahoma, Hlth. Sci. Ctr., Coll. of Pharm., P.O.
Box 26901, Oklahoma City, OK 93710, USA
SOURCE: Drugs of Today (Spain), (Aug 1989) Vol. 25, pp.
518-523. 34 Refs.
CODEN: MDACAP. ISSN: 0025-7656.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 89:7299
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB The description, pharmacological action, clinical evaluation for the adjunctive treatment on the management of signs and symptoms of

Parkinson's disease, adverse effects, and dosage and administration of pergolide mesylate are reviewed.
Victor Origoni

L9 ANSWER 254 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1989:1668 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 27-03204
TITLE: Pergolide and selegiline for Parkinson's disease
AUTHOR(S): anon
SOURCE: Medical Letter on Drugs and Therapeutics (USA), (Sep 8 1989) Vol. 31, pp. 81-83. 16 Refs.
CODEN: MELEAP. ISSN: 0025-732X.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 89:5438
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB The pharmacology, pharmacokinetics, clinical effectiveness, adverse effects and dosage of 2 newly approved antiparkinson agents, pergolide mesylate (Permax) and selegiline hydrochloride (Eldepryl) are reported.
Victor Origoni

L9 ANSWER 255 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 196
ACCESSION NUMBER: 1989:54391 BIOSIS
DOCUMENT NUMBER: PREV198987030391; BA87:30391
TITLE: PERGOLIDE LONG-TERM USE IN PARKINSON'S DISEASE.
AUTHOR(S): AHLSSKOG J E [Reprint author]; MUENTER M D
CORPORATE SOURCE: DEP NEUROL, MAYO CLINIC, ROCHESTER, MINN 55905, USA
SOURCE: Mayo Clinic Proceedings, (1988) Vol. 63, No. 10, pp. 979-987.
CODEN: MACPAJ. ISSN: 0025-6196.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 7 Jan 1989
Last Updated on STN: 7 Jan 1989

AB Previous short-term studies have shown that the dopamine agonist pergolide improves control of Parkinson's disease when used in conjunction with carbidopa-levodopa (Sinemet). We assessed the long-term outcome (2 1/2- to 3-year follow-up) in patients with Parkinson's disease who participated in our previous pergolide double-blind trial and were subsequently switched to open-label pergolide therapy. Of 41 evaluable patients who began pergolide therapy, 10 (24%) experienced sustained substantial benefit that persisted to the end of this investigation. A total of 23 patients (56%) remained on pergolide therapy and, as a group, had considerable improvement over baseline at 2 1/2 to 3 years on the basis of several measurements of efficacy. A tendency toward deterioration could be reversed in many patients by larger or more frequent doses of carbidopa-levodopa; nevertheless, all but four patients were still taking the same dose or less of cardidopa-levodopa at the end of this study as at the onset. Patients with the best initial response to pergolide seemed most likely to experience long-term benefit. Confusion and hallucinations were the side effects most likely to necessitate discontinuation of pergolide. Symptoms suggestive of dose-related angina pectoris occurred in four patients in the open-label phase and two patients win the earlier double-blind phase (13% of patients who started pergolide therapy); these symptoms were

easily controlled by dose reduction or discontinuation of pergolide, without sequelae. Dose-related leukopenia developed in one patient.

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ACCESSION NUMBER: 1989:54390 BIOSIS
DOCUMENT NUMBER: PREV198987030390; BA87:30390
TITLE: TREATMENT OF PARKINSON'S DISEASE WITH PERGOLIDE A
DOUBLE-BLIND STUDY.
AUTHOR(S): AHLISKOG J E [Reprint author]; MUENTER M D
CORPORATE SOURCE: DEP NEUROL, MAYO CLINIC, ROCHESTER, MINN 55905, USA
SOURCE: Mayo Clinic Proceedings, (1988) Vol. 63, No. 10,
pp. 969-978.
CODEN: MACPAJ. ISSN: 0025-6196.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 7 Jan 1989
Last Updated on STN: 7 Jan 1989

AB Pergolide is a potent dopamine agonist and is known to have anti-Parkinson properties. We administered pergolide to patients with suboptimal control of Parkinson's disease who had a short-duration response to carbidopa-levodopa in a 6-month, double-blind study. Pergolide added to the carbidopa-levodopa regimen resulted in both subjective and objective improvement in comparison with placebo. In patients who tolerated pergolide, the median time spent in the "off" (parkinsonian) state was reduced from 5.0 to 2.2 hours daily (compared with a 0.3-hour reduction in the placebo group). These patients were able to decrease the median frequency of carbidopa-levodopa dosage from 7.5 to 5.0 doses daily (no change in the placebo group). Prolongation of the "on" response (optimal response to treatment) to single doses of drugs was corroborated by monitoring of the patients' Parkinson response cycle. The peak response was also improved in most patients. Of 25 patients randomized to the pergolide group, 7 were unable to tolerate this drug; confusion or hallucinations occurred in 4 of these patients, and chest pain, leukopenia, and nonspecific dizziness, respectively, developed in the other 3. All adverse events were reversible with reduction of the dose or discontinuation of the pergolide regimen. In conclusion, patients with Parkinson's disease who experience clinical fluctuations with carbidopa-levodopa may be helped by the addition of pergolide to the therapeutic regimen.

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ACCESSION NUMBER: 1989030619 EMBASE
TITLE: Intracerebroventricular infusion of dopamine and its agonists in rodents and primates. An experimental approach to the treatment of Parkinson's disease.
AUTHOR: Garcia de Yebenes, J.; Fahn, S.; Mena, M.A.; Pardo, B.; Casarejos, M.J.
CORPORATE SOURCE: Departamento de Investigacion, Centro 'Ramon y Cajal', Madrid 28034, Spain.
SOURCE: ASAI0 Transactions, (1988) Vol. 34, No. 4, pp. 951-957.
ISSN: 0889-7190 CODEN: ASATEJ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
030 Clinical and Experimental Pharmacology

037 Drug Literature Index
008 Neurology and Neurosurgery

LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Dec 1991
Last Updated on STN: 12 Dec 1991

AB The authors investigated the effects of chronic intracerebroventricular (ICV) infusion of dopamine (DA) and DA agonists in animal models of DA deficiency in rodents and primates. Rats with unilateral nigrostriatal lesions induced by 6-OH-DA received infusions of DA, pergolide, lisuride, and (+)-4-propyl-9-hydroxynaphthoxacine (PHNO) for from 1 to 2 weeks through a catheter implanted into the cerebral ventricle ipsilateral to the lesion and connected to an osmotic minipump filled with the active substance. The infused animals had persistent contralateral rotation during the period of infusion. The DA infusion restored DA levels in lesioned animals. In animals treated chronically with reserpine, the ICV DA infusion restored DA levels in the brain, but akinesia was not reversed unless monoamine oxidase inhibitors were also given, intraperitoneally or ICV, with the DA infusion. An ICV infusion of PHNO reversed reserpine-induced akinesia. The infusion of DA or PHNO restored normal patterns of behavior in monkeys made akinetic by treatment with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), but the infusion was complicated by intolerance to the pump or frequent disconnection of the catheter. An ICV infusion of PHNO may be an alternative experimental approach to the treatment of fluctuations in patients with Parkinson's disease.

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STN DUPLICATE 199

ACCESSION NUMBER: 1988:312440 BIOSIS
DOCUMENT NUMBER: PREV198886029478; BA86:29478
TITLE: PARKINSON'S DISEASE AN OPEN LABEL TRIAL OF PERGOLIDE IN
PATIENTS FAILING BROMOCRIPTINE THERAPY.
AUTHOR(S): FACTOR S A [Reprint author]; SANCHEZ-RAMOS J R; WEINER W J
CORPORATE SOURCE: UNIV MIAMI SCH MED, DEP NEUROL D4-5 , PO BOX 016960, MIAMI,
FLORIDA 33101, USA
SOURCE: Journal of Neurology Neurosurgery and Psychiatry, (
1988) Vol. 51, No. 4, pp. 529-533.
CODEN: JNNPAU. ISSN: 0022-3050.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 3 Jul 1988
Last Updated on STN: 3 Jul 1988

AB Sixty-three patients with Parkinson's disease who failed bromocriptine therapy for various reasons were treated in an open-label trial of pergolide. The data were evaluated in a retrospective manner. Forty-six percent had a good response and tolerated the pergolide. A comparison of the outcomes regarding response and toxicity revealed that bromocriptine and pergolide act differently in individual patients. A trial of pergolide in Parkinsonian patients failing bromocriptine therapy may be therapeutically useful.

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STN DUPLICATE 200

ACCESSION NUMBER: 1988:443543 BIOSIS
DOCUMENT NUMBER: PREV198886095641; BA86:95641
TITLE: COMPARATIVE EFFICACY OF TWO DOPAMINE AGONISTS PERGOLIDE AND
LERGOTRILE IN PARKINSON DISEASE.
AUTHOR(S): LIEBERMAN A N [Reprint author]; GOLDSTEIN M; LEIBOWITZ M
CORPORATE SOURCE: NY UNIV SCH MED, 650 FIRST AVE, NEW YORK, NY 10016, USA

SOURCE: New York State Journal of Medicine, (1988) Vol.
88, No. 8, pp. 420-422.
CODEN: NYSJAM. ISSN: 0028-7628.

DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 4 Oct 1988
Last Updated on STN: 4 Oct 1988

AB Pergolide is a dopamine agonist that will soon be available for the treatment of Parkinson disease (PD). Pergolide is a congener of an older agonist; lergotrile. Lergotrile, an effective antiparkinson drug, was withdrawn from the market because it resulted in hepatotoxicity in up to one third of patients. Pergolide differs from lergotrile in the presence of a propyl group on the N6 portion of the ergoline molecule. In animal models of PD, this substitution increases the antiparkinsonian effect. Pergolide also lacks lergotrile's cyano and halogen groups. These groups may be responsible for lergotrile's hepatotoxicity. The activity of pergolide and lergotrile was compared in a retrospective analysis of 12 patients with advanced PD who were no longer satisfactorily responding to levodopa. Lergotrile or pergolide was added to the levodopa regimen. Pergolide was at least as effective as lergotrile. Unlike lergotrile, pergolide was not hepatotoxic. The mean dose of lergotrile was 50.4 mg. The mean dose of pergolide was 2.2 mg. This study demonstrates that a drug's structure can be modified in a rational manner with the new drug retaining the old drug's efficacy but not its toxicity.

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STN DUPLICATE 201

ACCESSION NUMBER: 1988:289395 BIOSIS
DOCUMENT NUMBER: PREV198886017662; BA86:17662
TITLE: DOPAMINERGIC EFFECTS ON KIDNEY FUNCTION AND RESPONSIVENESS
OF ALDOSTERONE PLASMA RENIN ACTIVITY PROLACTIN
CATECHOLAMINES AND BLOOD PRESSURE TO STIMULATION IN
PATIENTS WITH PROLACTINOMA COMPARISON OF THE EFFICACY OF
PERGOLIDE AND BROMOCRIPTINE THERAPY.

AUTHOR(S): JUNGSMANN E [Reprint author]; HAAK T; ALTHOFF P-H;
FASSBINDER W; SCHOEFFLING K

CORPORATE SOURCE: ABTEILUNG ENDOKRINOL, ZENTRUM INNEREN MED, KLINIKUM JOHANN
WOLFGANG GOETHE-UNIV, THEODOR-STERN-KAI 7, D-6000
FRANKFURT/MAIN 70, FRG

SOURCE: Arzneimittel-Forschung, (1988) Vol. 38, No. 2,
pp. 296-300.
CODEN: ARZNAD. ISSN: 0004-4172.

DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 16 Jun 1988
Last Updated on STN: 16 Jun 1988

AB β -[(Methylthio)methyl]-6-propylergoline (pergolide) is a new, potent, long-acting dopaminergic DA2 receptor agonist currently being investigated for therapeutic use in patients with hyperprolactinemia, acromegaly or Parkinson's disease. Since the influence of bromocriptine, a well-established dopaminomimetic compound, on aldosterone responsiveness and plasma renin activity is still a matter of debate, the efficacies of both compounds on these parameters and on kidney function, blood pressure, catecholamine release and prolactin levels were compared in 16 patients with prolactinoma. Supine and furosemide (40 mg i.v.)-stimulated plasma renin activity and aldosterone levels were similarly decreased by bromocriptine (2.5-30 mg/d) and pergolide (50-500 mg/d). Suppression of blood pressure, inhibition of stimulated

norepinephrine release, increase in creatinine clearance, and decrease in base-line prolactin levels were similarly pronounced during treatment with both compounds. Metoclopramide (10 mg i.v.)-induced stimulation of aldosterone and prolactin levels, however, were suppressed only by bromocriptine and not by pergolide. It remains to be studied whether this difference between bromocriptine and pergolide is due to a potential agonist effect of pergolide on dopaminergic DA1 receptors which are influenced by bromocriptine in an antagonistic manner, or whether pergolide can be more readily displaced from its receptors than bromocriptine.

L9 ANSWER 261 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 202
ACCESSION NUMBER: 1988:505250 CAPLUS
DOCUMENT NUMBER: 109:105250
ORIGINAL REFERENCE NO.: 109:17409a,17412a
TITLE: D1 and D2 dopamine receptor mechanisms in dopaminergic behaviors
AUTHOR(S): Koller, William C.; Herbster, Gregory
CORPORATE SOURCE: Med. Cent., Univ. Kansas, Kansas City, KS, 66103, USA
SOURCE: Clinical Neuropharmacology (1988), 11(3), 221-31
CODEN: CLNEDB; ISSN: 0362-5664
DOCUMENT TYPE: Journal
LANGUAGE: English

AB SKF 38393, a selective D1 dopamine receptor agonist, was investigated when administered alone and in combination with dopaminergic agonists in animal models of extrapyramidal behavior. SKF 38393 did not induce stereotypy in normal rats but enhanced apomorphine-induced stereotypy in a dose-dependent manner. SKF 38393 also augmented and altered the stereotypic response of dopaminergic agonists (+)-4-propylhydronaphthoxazine (PHNO), quinpirole, and ciladopa. The addition of SKF 38393 with ciladopa changed the behavioral response of ciladopa from a partial to a full agonist. SKF 38393 did not alter locomotor behavior; however, it augmented the stimulatory but not the inhibitory response of apomorphine on locomotion. In unilateral 6-hydroxydopamine-lesioned animals, SKF 38393 caused contralateral rotation that were similar to those of other dopaminergic agonists. The addition of SKF 38393 to both mixed D1/D2 (levodopa, pergolide) and selective D2 (PHNO, quinpirole) dopamine agonists resulted in a synergistic rather than an additive effect. No changes in behavior were observed in rats challenged with apomorphine after being treated 21 days with SKF 38393, PHNO, SKF 38393 plus PHNO, or saline. D1 agonism is capable of augmenting and altering dopaminergic behavior of both mixed D1/D2 and D2 dopamine receptor agonists. A combination of D1 and D2 dopamine agonists may represent optimal drug treatment for Parkinson's disease.

OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

L9 ANSWER 262 OF 331 MEDLINE on STN DUPLICATE 203
ACCESSION NUMBER: 1988300025 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2900291
TITLE: Receptor changes during chronic dopaminergic stimulation.
AUTHOR: Jenner P; Boyce S; Marsden C D
CORPORATE SOURCE: University Department of Neurology, Institute of Psychiatry, London, U.K.
SOURCE: Journal of neural transmission. Supplementum, (1988) Vol. 27, pp. 161-75. Ref: 46
Journal code: 0425126. ISSN: 0303-6995.
PUB. COUNTRY: Austria
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198809
ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 6 Feb 1995
Entered Medline: 16 Sep 1988

AB The underlying cause of the long term complications of L-DOPA or dopamine agonist therapy in Parkinson's disease remains unknown. Previous studies of repeated administration of L-DOPA or bromocriptine to rodents have shown increases, decreases or no change in brain dopaminergic activity. For this reason we have re-examined the effects of chronic L-DOPA or dopamine agonist administration on brain dopamine receptor function in rats. Repeated intraperitoneal administration of L-DOPA to rats for 21 days followed by 3 days drug withdrawal caused an enhancement of apomorphine-induced stereotypy but no apparent alteration in striatal dopamine receptor numbers or affinity (as judged by 3H-spiperone; 3H-NPA and 3H-piflutixol binding). Chronic oral administration of L-DOPA plus carbidopa to rats for one year was without effect on apomorphine-induced stereotypy or striatal D-2 dopamine receptors. Similarly, no effects were observed on striatal dopamine function following one year's administration of bromocriptine. Pergolide produced an enhancement of apomorphine-induced stereotypy but a decrease in D-2 receptor density as judged by 3H-spiperone binding. In rats with a unilateral 6-OHDA lesion of the medial forebrain bundle the oral administration of L-DOPA plus carbidopa for 4 weeks, followed by 4 days withdrawal, enhanced the rate of apomorphine-induced contraversive rotation. It appears difficult, at least in rats, to manipulate striatal dopamine receptors with L-DOPA or dopamine agonist drugs. An enhancement of motor behaviour can occur in the presence of no change or a decrease in dopamine receptor numbers identified by in vitro ligand binding to tissue homogenates.

L9 ANSWER 263 OF 331 MEDLINE on STN DUPLICATE 204

ACCESSION NUMBER: 1988300024 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3165432
TITLE: Continuous intracerebroventricular infusion of dopamine and dopamine agonists through a totally implanted drug delivery system in animal models of Parkinson's disease.
AUTHOR: de Yebenes J G; Fahn S; Jackson-Lewis V; Jorge P; Mena M A; Reiriz J
CORPORATE SOURCE: Centro Ramon y Cajal, Madrid, Spain.
SOURCE: Journal of neural transmission. Supplementum, (1988) Vol. 27, pp. 141-60.
Journal code: 0425126. ISSN: 0303-6995.
PUB. COUNTRY: Austria
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198809
ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 6 Feb 1998
Entered Medline: 16 Sep 1988

AB We studied the effect of intracerebroventricular infusion of dopamine and dopamine agonists in animal models of dopamine deficiency as an experimental approach to the treatment of levodopa induced fluctuations in Parkinson's disease. Dopamine deficiency was produced in rats by unilateral lesion of the nigrostriatal pathway or by chronic treatment with reserpine. Monkeys were lesioned by intravenous injection of MPTP. The animals were treated with intracerebral infusions of dopamine (with or without associated intraperitoneal administration or intracerebroventricular infusion of pargyline), lisuride and pergolide. The intracerebroventricular infusion of these drugs

was performed with osmotic minipumps in rats and with infusaid pumps in the monkeys. The infusion of dopamine or dopamine agonists in rats with unilateral lesions by 6-OH-dopamine produced a persistent rotation contralateral to the lesioned and implanted side. The infusion of dopamine reversed reserpine-induced akinesia only when pargyline was associated. In the range of concentration used, maximum allowed by solubility of compounds, the effects of dopamine were more potent than those of the agonists. In spite of the stability of dopamine "in vitro" when dissolved in antioxidants and at low pH, a pigment, product of autooxidation, was found in the brains of the animals infused with dopamine. The monkeys were implanted with infusaid pumps and infused for up to 3 weeks. The pump was not well tolerated due to its huge size for the animals. One monkey showed reversal of the MPTP-induced akinesia while the other, whose catheter had moved from the correct implantation site, remained unchanged. In both monkeys there was evidence of autooxidation of dopamine. Intracerebral infusion of dopamine agonists may be a possible experimental alternative to the treatment of levodopa induced fluctuations in Parkinson's disease but stable and soluble dopamine agonists and suitable delivery systems are needed.

L9 ANSWER 264 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 205

ACCESSION NUMBER: 1989:185752 CAPLUS

DOCUMENT NUMBER: 110:185752

ORIGINAL REFERENCE NO.: 110:30634h,30635a

TITLE: Effect of 12 months continuous administration of levo-3,4-dihydroxyphenylalanine, bromocriptine, or pergolide on striatal dopamine function in rats

AUTHOR(S): Boyce, S.; Jenner, P.; Marsden, C. D.

CORPORATE SOURCE: Dep. Neurol., Univ. London, London, UK

SOURCE: Neurology and Neurobiology (1988), 42B(Progr. Catecholamine Res., Pt. B), 113-16
CODEN: NEUND9; ISSN: 0736-4563

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effect of antiparkinsonian drugs (L-dopa, bromocriptine and pergolide) on brain dopaminergic function was studied. Chronic treatment with L-DOPA or bromocriptine does not readily alter striatal dopamine (DA) function. Pergolide altered the behavioral effects elicited by acute challenge with the DA agonist apomorphine, producing an exaggerated response, associated with diminished DA D2 receptor number. The relations of these results to observed behavioral side-effects in parkinson's patients after chronic treatment with dopaminergic drugs are considered.

L9 ANSWER 265 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1988:2925 TOXCENTER

COPYRIGHT: Copyright (c) 2009 The Thomson Corporation

DOCUMENT NUMBER: 26-11477

TITLE: Drugs for parkinsonism

AUTHOR(S): anon

SOURCE: Medical Letter on Drugs and Therapeutics (USA), (Dec 16 1988) Vol. 30, pp. 113-116.
CODEN: MELEAP. ISSN: 0025-732X.

DOCUMENT TYPE: Journal

FILE SEGMENT: IPA

OTHER SOURCE: IPA 88:10326

LANGUAGE: English

ENTRY DATE: Entered STN: 16 Nov 2001

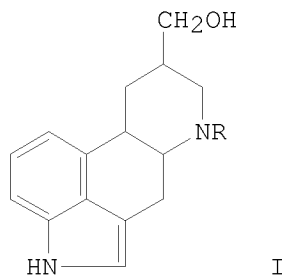
Last Updated on STN: 16 Nov 2001

AB The mechanism of action, clinical effects, limitations, and adverse effects of drugs used in the treatment of Parkinson disease are presented. Drugs covered include levodopa alone and in combination with

carbidopa (Sinemet), bromocriptine mesylate (Parlodel), anticholinergic agents, amantadine hydrochloride (Symmetrel), selegiline hydrochloride (Eldepryl), pergolide (Permax), lisuride, controlled release Sinemet, and adjunctive antidepressants.
Lisa Webster

L9 ANSWER 266 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1987:440177 CAPLUS
DOCUMENT NUMBER: 107:40177
ORIGINAL REFERENCE NO.: 107:6739a,6742a
TITLE: Decyanation of pergolide intermediate
INVENTOR(S): Misner, Jerry Wayne
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 213850	A2	19870311	EP 1986-306281	19860814 <--
EP 213850	A3	19880120		
EP 213850	B1	19920108		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
US 4782152	A	19881101	US 1985-766362	19850816 <--
IL 79711	A	19911121	IL 1986-79711	19860813 <--
CA 1296324	C	19920225	CA 1986-515847	19860813 <--
AT 71377	T	19920115	AT 1986-306281	19860814 <--
JP 62045587	A	19870227	JP 1986-191954	19860815 <--
JP 06070048	B	19940907		
HU 41777	A2	19870528	HU 1986-3600	19860815 <--
HU 196395	B	19881128		
PRIORITY APPLN. INFO.:			US 1985-766362	A 19850816
			EP 1986-306281	A 19860814
OTHER SOURCE(S):			CASREACT 107:40177	
GI				



AB 8 β -D-Ergoline-8-methanol (I; R = H) was prepared by decyanation of I (R = cyano) with an alkali hydroxide in an alc. solvent. I (R = H) is an intermediate for pergolide mesylate, a prolactin inhibitor and useful in treating Parkinsonism. I (R = cyano) was heated with NaOH in (HOCH₂)₂ at .apprx.125° to give 100% I (R = H). Pergolide mesylate (II) was prepared in 4 steps from I (R = H).

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD
(3 CITINGS)

L9 ANSWER 267 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 206

ACCESSION NUMBER: 1987:487881 BIOSIS
DOCUMENT NUMBER: PREV198784122524; BA84:122524
TITLE: PHARMACOLOGICAL CHARACTERISTICS OF TREMOR RIGIDITY AND
HYPOKINESIA INDUCED BY RESERPINE IN RAT.
AUTHOR(S): COLPAERT F C [Reprint author]
CORPORATE SOURCE: FONDAX-GROUPE RECH SERV, 7 RUE AMPERE, 92800 PUTEAUX, FR
SOURCE: Neuropharmacology, (1987) Vol. 26, No. 9, pp.
1431-1440.
CODEN: NEPHBW. ISSN: 0028-3908.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 17 Nov 1987
Last Updated on STN: 17 Nov 1987

AB The experiments characterized the dose- and time-dependence of parkinsonian motor signs induced by reserpine in rats and a standardized system of manipulation of animals, evaluation of symptoms and analysis of data was devised. The assay procedure yielded no more than 0.5, 4.5 and 0.0% false positives with the evaluation of tremor, rigidity and hypokinesia, respectively. A dose-dependent and often complete blockade of all three signs was obtained with L-DOPA plus carbidopa (10:1) as well as with other classes of pharmacological agents that are used in the treatment of Parkinson's disease, i.e., direct or indirect dopamine (DA) agonists (amantadine, pergolide, lisuride) and inhibitors of monoamine oxidase (MAO) (clorgyline, pargyline, deprenyl, tranlylcypromine). The inhibitor of the uptake of DA, nomifensine, and anticholinergics, 5-hydroxytryptamine (5-HT) antagonists, histamine antagonists and tricyclic antidepressants exerted little or no effect. The effects of putative agonists and antagonists at $\alpha 1$ - and $\alpha 2$ -adrenoceptors were also examined. Yohimbine blocked tremor and rigidity, but not hypokinesia, at 0.66 and 0.28 mg/kg, respectively. It is suggested that alpha-adrenergic mechanisms, and in particular, $\alpha 2$ -adrenoceptors, may be involved in reserpine-induced tremor and rigidity. Noradrenergic and dopaminergic systems can conceivably interact to progressively generate these different motor signs.

L9 ANSWER 268 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 207

ACCESSION NUMBER: 1987:298528 BIOSIS
DOCUMENT NUMBER: PREV198784028560; BA84:28560
TITLE: MESULERGINE AND PERGOLIDE IN PREVIOUSLY UNTREATED
PARKINSON'S DISEASE.
AUTHOR(S): WRIGHT A [Reprint author]; LEES A J; STERN G M
CORPORATE SOURCE: DEP NEUROL, MIDDLESEX HOSP, MORTIMER ST, LONDON W1N 8AA, UK
SOURCE: Journal of Neurology Neurosurgery and Psychiatry, (1987) Vol. 50, No. 4, pp. 482-484.
CODEN: JNNPAU. ISSN: 0022-3050.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 6 Jul 1987
Last Updated on STN: 6 Jul 1987

AB Seventeen hitherto untreated patients with mild Parkinson's disease were given the dopamine agonists mesulergine or pergolide. Of the 10 patients who received pergolide (mean dosage 3.7 mg/day) five failed to improve, four showed slight improvement and one gained moderate benefit. Of the seven patients who received mesulergine (mean dose 6.4 mg/day) three patients derived no benefit, two slight benefit and two moderate benefit. The incidence of adverse side-effects was high with both drugs despite the use of a peripheral dopamine receptor

antagonist, domperidone, when required. These results are less encouraging than those reported from other centres both in respect of response rate and the severity of unwanted effects.

L9 ANSWER 269 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 208

ACCESSION NUMBER: 1987215136 EMBASE
TITLE: Update on dopamine agonists in Parkinson's disease: 'Beyond bromocriptine'.
AUTHOR: Lang, A.E.
CORPORATE SOURCE: Movement Disorders Clinic, Toronto Western Hospital, Toronto, Ont. M5T 2R2, Canada.
SOURCE: Canadian Journal of Neurological Sciences, (1987) Vol. 14, No. 3 SUPPL., pp. 474-482.
ISSN: 0317-1671 CODEN: CJNSA2
COUNTRY: Canada
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: French

AB Since the initiation of bromocriptine therapy for Parkinson's disease several newer dopamine agonists have been developed. Pergolide has reached the stage of Phase 3 clinical trials and will probably be available for general use sometime in the foreseeable future. Lisuride shows most promise in its parenteral form for infusion therapy of patients with severe fluctuations. Mesulergine, another ergot-derivative and ciladopa, a new non-ergot agonist, have been withdrawn from further clinical use due to tumorigenesis in rats. It is questionable how applicable these findings are to the use of the drugs in elderly humans with parkinsonism. Recently a small number of drugs have been found to have postsynaptic dopamine agonist properties only in the setting of denervated supersensitive dopamine receptors. These agents may be particularly effective in the early treatment of patients with Parkinson's disease. This paper will review a number of the dopamine agonists which have been developed since the introduction of bromocriptine therapy. Several of these have shown beneficial effects in early clinical trials while others show promise in preclinical studies of animal models of parkinsonism.

L9 ANSWER 270 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 209

ACCESSION NUMBER: 1987215135 EMBASE
TITLE: D-1 and D-2 agonists in Parkinson's disease.
AUTHOR: Lieberman, A.N.; Goldstein, M.; Gopinathan, G.; Neophytides, A.
CORPORATE SOURCE: New York University School of Medicine, Beekman Downtown Medical Center, New York, NY, United States.
SOURCE: Canadian Journal of Neurological Sciences, (1987) Vol. 14, No. 3 SUPPL., pp. 466-473.
ISSN: 0317-1671 CODEN: CJNSA2
COUNTRY: Canada
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: French

AB We have evaluated 5 DA agonists-bromocriptine, lergotrile, lisuride,

pergolide and mesulergine in studies encompassing 278 patients with advanced PD. In most of our patients the DA agonist was added to levodopa. Most of our patients were no longer satisfactorily responding to levodopa. Previous attempts at managing these patients by changing the dose of levodopa (increasing or decreasing it), the treatment schedule, or the ratio of levodopa to carbidopa or by temporarily discontinuing levodopa [drug holiday] were unsuccessful. The majority of our patients had diurnal fluctuations in performance, either 'wearing off' or 'on-off' phenomena. The addition of a DA agonist resulted in a decrease in parkinsonian disability in most patients and a decrease in the severity of the diurnal fluctuations in performance. Improvement in many patients was maintained for at least 2 years. Adverse effects included mental changes, dyskinesias, orthostatic hypotension, and nausea. All of the adverse effects were reversible when the agonist was decreased or discontinued. As a group the agonists behaved similarly but individual patients often responded better to one agonist than another. The main role of agonists is in combination with levodopa in the treatment of patients with early PD who have not yet developed dyskinesias or diurnal fluctuations in performance.

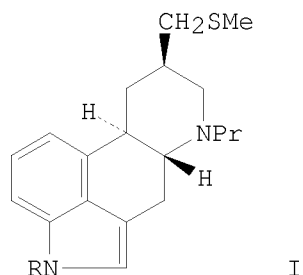
L9 ANSWER 271 OF 331 MEDLINE on STN DUPLICATE 210
 ACCESSION NUMBER: 1989070564 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 2904648
 TITLE: Continuous intracerebroventricular infusion of dopamine and dopamine agonists through a totally implanted drug delivery system in animal models of Parkinson's disease.
 AUTHOR: de Yebenes J G; Fahn S; Lovelle S; Jackson-Lewis V; Jorge P; Mena M A; Reiriz J; Bustos J C; Magarinos C; Martinez A
 CORPORATE SOURCE: Department of Neurology, Columbia University College of Physicians & Surgeons, New York, NY.
 SOURCE: Movement disorders : official journal of the Movement Disorder Society, (1987) Vol. 2, No. 3, pp. 143-58.
 Journal code: 8610688. ISSN: 0885-3185.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198901
 ENTRY DATE: Entered STN: 8 Mar 1990
 Last Updated on STN: 3 Mar 2000
 Entered Medline: 19 Jan 1989

AB We studied the effect of intracerebroventricular infusion of dopamine and dopamine agonists in rat and primate models of Parkinson's disease as an experimental approach to the treatment of levodopa-induced fluctuations. The infusion of dopamine, lisuride, and pergolide into the ventricle ipsilateral to the lesion, by 6-hydroxydopamine, of the nigrostriatal pathway induced a contralateral rotation which was maximal 24-48 h after infusion and whose intensity progressively decreased over the period of 1 week. [3H]Spiperone binding was decreased by the infusion of dopamine but the responses to subcutaneous apomorphine were unchanged. The infusion of dopamine also restored the levels of monoamines in the rat brain. In chronic reserpized rats, the infusion of dopamine restored brain levels of dopamine but did not reverse akinesia unless monoamine oxidase inhibitors were simultaneously administered, either systemically or intracerebroventricularly. Lisuride and pergolide proved much weaker than dopamine in reversing the effects of reserpine. Intracerebroventricular infusion of dopamine plus deprenyl reversed MPTP induced akinesia in monkeys but the pump used for the delivery was not well tolerated, because of its size, by the animals.

L9 ANSWER 272 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1986:534217 CAPLUS
DOCUMENT NUMBER: 105:134217
ORIGINAL REFERENCE NO.: 105:21673a,21676a
TITLE: Ergoline derivatives
INVENTOR(S): Laguzza, Bennet Coleman
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 185491	A1	19860625	EP 1985-308835	19851204 <--
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
US 4675322	A	19870623	US 1984-679832	19841210 <--
JP 61140584	A	19860627	JP 1985-275849	19851206 <--
PRIORITY APPLN. INFO.:			US 1984-679832	A 19841210
OTHER SOURCE(S):	CASREACT 105:134217; MARPAT 105:134217			
GI				



AB The title compds. I [R = MeCH:CH, H2C:CHCH2, C1-3 alkyl, (un)substituted PhCH2] and their salts, useful as dopamine D-2 agonists capable of lowering blood pressure, were prepared Thus, pergolide mesylate in DMF was treated with KOCMe3, followed by MeI to give I (R = Me) (II). II at 50 µg/kg, i.p. in rats gave 81% prolactin inhibition, at 1 mg/kg resulted in 86 turns (Parkinsonism test) and at 100 µg/kg resulted in -21% change in mean arterial blood pressure. A hard gelatin capsule formulation contained I 0.1-20, dried starch 200, and Mg stearate 10 mg.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L9 ANSWER 273 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 211

ACCESSION NUMBER: 1986:364549 BIOSIS
DOCUMENT NUMBER: PREV198682069023; BA82:69023
TITLE: DOUBLE-BLIND ASSESSMENT OF POTENTIAL PERGOLIDE-INDUCED CARDIOTOXICITY.
AUTHOR(S): KURLAN R [Reprint author]; MILLER C; KNAPP R; MURPHY G; SHOULSON I
CORPORATE SOURCE: UNIVERSITY OF ROCHESTER MEDICAL CENTER, 601 ELMWOOD AVENUE, BOX 573, ROCHESTER NY 14642, USA
SOURCE: Neurology, (1986) Vol. 36, No. 7, pp. 993-995.
CODEN: NEURAI. ISSN: 0028-3878.

DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 6 Sep 1986
Last Updated on STN: 6 Sep 1986

AB Possible pergolide-induced cardiotoxicity has been reported in open trials. Over a 6-month period of observation, we prospectively analyzed ECGs and 24-hour ambulatory ECG in 23 patients with Parkinson's disease who were randomized in a double-blind fashion to pergolide or placebo treatments. Pergolide therapy was associated with a mild and transient bradycardiac effect, but no clinically significant cardiotoxicity.

L9 ANSWER 274 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1987:12900 CAPLUS
DOCUMENT NUMBER: 106:12900
ORIGINAL REFERENCE NO.: 106:2129a,2132a
TITLE: Alterations in [Met5]- and [Leu5]enkephalin and neurotensin content in basal ganglia induced by the long-term administration of dopamine agonist and antagonist drugs to rats
AUTHOR(S): De Ceballos, Maria L.; Boyce, Susan; Jenner, Peter; Marsden, C. David
CORPORATE SOURCE: Med. Sch., King's Coll. Hosp., London, UK
SOURCE: European Journal of Pharmacology (1986), 130(3), 305-9
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Treatment of rats for 18 mo with trifluoperazine [117-89-5] increased [Met5]- [58569-55-4] and [Leu5]enkephalin [58822-25-6] and neurotensin [39379-15-2] content in the striatum and nucleus accumbens. However, in the substantia nigra the content of [Met5]enkephalin was decreased, [Leu5]enkephalin unchanged, and that of neurotensin increased. Administration of L-DOPA [59-92-7] plus carbidopa [28860-95-9], bromocriptine mesylate [22260-51-1] or pergolide mesylate [66104-23-2] 12 mo decreased [Met5]enkephalin (except bromocriptine) and neurotensin, but not [Leu5]enkephalin, levels in striatum. L-DOPA decreased and bromocriptine increased neurotensin levels in the substantia nigra. Neurotensin levels in nucleus accumbens were unaffected. Thus, alterations in brain neuropeptides observed in Parkinson's disease may be related both to the pathol. of the disease and to its treatment.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD
(3 CITINGS)

L9 ANSWER 275 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1986:2088 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 24-08436
TITLE: Therapeutic progress. Review 20. Drug treatment of Parkinson's disease
AUTHOR(S): Pall, H. S.; Williams, A. C.; Ramsden, D. B.
CORPORATE SOURCE: Dept. of Neurology, Queen Elizabeth Hosp., Birmingham B15 2TH, England
SOURCE: J. Clin. Hosp. Pharm., (Aug 1986) Vol. 11, pp. 229-236. 31 Refs.
CODEN: JCHPDS. ISSN: 0143-3180.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 86:6962
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001

Last Updated on STN: 16 Nov 2001

AB Guidelines for the prevention and therapy of Parkinson disease are discussed. The avoidance of overprescribing with phenothiazines, butyrophenones and thioxanthenes is noted. Use of levodopa, dopamine agonists (bromocriptine; lisuride; pergolide), parasympatholytic agents and antidepressants is categorized.
Paul R. Webster

L9 ANSWER 276 OF 331 MEDLINE on STN DUPLICATE 212

ACCESSION NUMBER: 1986217821 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3708601
TITLE: Long-term efficacy of pergolide in patients with Parkinson's disease.
AUTHOR: Sage J I; Duvoisin R C
SOURCE: Clinical neuropharmacology, (1986) Vol. 9, No. 2, pp. 160-4.
Journal code: 7607910. ISSN: 0362-5664.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198607
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 21 Mar 1990
Entered Medline: 7 Jul 1986

AB We report the clinical course of 35 patients with Parkinson's disease who experienced an initially favorable response to pergolide and who were taking the drug for at least 6 months. The duration of pergolide treatment was 6-50 (25 +/- 16 SD) months. Of the 14 patients who remained on pergolide for over 2 years, 12 remained less disabled for 26 +/- 17 SD months, seven enjoyed increased "on" time for 39 +/- 8 SD months, and nine had a lower Hoehn-Yahr stage for 25 +/- 17 SD months. Pergolide was discontinued after 5-39 months in eight patients; six patients then deteriorated. Pergolide can remain efficacious in the treatment of Parkinson's disease for up to 50 months.

L9 ANSWER 277 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 213

ACCESSION NUMBER: 1986:213855 BIOSIS
DOCUMENT NUMBER: PREV198681105155; BA81:105155
TITLE: EFFICACY OF PERGOLIDE AND MESULERGINE.
AUTHOR(S): LIEBERMAN A N [Reprint author]; GOPINATHAN G; NEOPHYTIDES A
CORPORATE SOURCE: 530 FIRST AVE NB 7W15, NEW YORK, NY 10016, USA
SOURCE: European Neurology, (1986) Vol. 25, No. 2, pp. 86-90.
CODEN: EUNEAP. ISSN: 0014-3022.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 28 May 1986
Last Updated on STN: 28 May 1986

AB The activity of pergolide, a clavine ergolene, and mesulergine, an 8-alpha amino ergoline, were compared in 18 patients with advanced Parkinson's disease. All of the patients were no longer satisfactorily responding to levodopa, and 16 patients had diurnal oscillations in performance. Pergolide, mean dose 2.7 mg, when added to levodopa resulted in a significant (27%) decrease in Parkinson disability and a significant improvement in diurnal oscillations in performance (136% increase in hours 'on'). Twelve of the 18 patients (67%) improved. However, after 2 years pergolide was discontinued in all of the patients because of decreased efficacy,

adverse effects, or both. At this time, mesulergine, mean dose 9.3 mg., when added to levodopa resulted in a significant (37%) decrease in Parkinson disability and a significant improvement in diurnal oscillations (61% increase in hours 'on'). Twelve of the 18 patients (67%) improved. Adverse effects (dyskinesias) were less with mesulergine than with pergolide. A declining response to one agonist does not preclude a successful response to another agonist of a different class.

L9 ANSWER 278 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1986:1126 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 24-02663
TITLE: Investigational drug data: pergolide
AUTHOR(S): Briceland, L. L.
CORPORATE SOURCE: School of Pharm., State Univ. of New York at Buffalo, Amherst, NY
SOURCE: New York State Journal of Pharmacy, (1986) Vol. 6, pp. 10-11. 12 Refs.
ISSN: 0279-8778.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 86:3105
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB The pharmacology, pharmacokinetics, clinical trials, and adverse effects of the investigational drug pergolide are discussed. The antiparkinsonian action of I as well as inhibition of prolactin secretion have led to the investigational use of I in the treatment of Parkinson disease and hyperprolactinemic syndromes.
Anne L. Morisseau

L9 ANSWER 279 OF 331 MEDLINE on STN

ACCESSION NUMBER: 1987244089 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3297319
TITLE: Management of levodopa failures: the use of dopamine agonists.
AUTHOR: Lieberman A N; Gopinathan G; Neophytides A; Goldstein M
SOURCE: Clinical neuropharmacology, (1986) Vol. 9 Suppl 2, pp. S9-21. Ref: 70
Journal code: 7607910. ISSN: 0362-5664.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198707
ENTRY DATE: Entered STN: 5 Mar 1990
Last Updated on STN: 5 Mar 1990
Entered Medline: 31 Jul 1987

AB In the past decade, dopamine agonists have emerged as important treatment options for patients with Parkinson's disease. Originally, dopamine agonists were used only in patients with advanced disease in whom the response to levodopa had decreased (levodopa failures). The decreased response to levodopa, usually associated with diurnal oscillations in performance and the 'wearing-off' and 'on-off' phenomena, is secondary to disease progression with continued degeneration of the nigrostriatal neurons. In addition, chronic levodopa treatment itself may contribute to the decreased drug response and the diurnal oscillations in performance. Dopamine receptor agonists bypass the degenerating nigrostriatal neurons and directly stimulate the striatal dopamine receptors. Dopamine receptor

agonists also permit a reduction in the dose of levodopa. Five ergoline dopamine agonists--bromocriptine, lergotrile, pergolide, lisuride, mesulergine, and the nonergoline agonist, ciladopa--have undergone clinical trials in Parkinson's disease. In 10 years, we treated a total of 278 patients with advanced Parkinson's disease, a declining response to levodopa, and diurnal oscillations in performance with five ergoline dopamine agonists (in addition to levodopa). The mean duration of treatment was one year (with a range of 1-60 months). Improvement was noted in 140 (50%) of our patients. Adverse effects necessitating discontinuation of the agonist occurred in 131 patients (46%). We compared our results with those of others who, unlike us, began treatment with a dopamine agonist earlier, using the agonist alone or adding it to levodopa before the response to levodopa had decreased. Many of the patients so treated had mild or moderate Parkinson's disease. A total of 1,599 patients were treated with ergoline dopamine agonists. Of these patients, 976 (61%) improved, while 407 (25%) experienced adverse effects. We believe that a greater number of these patients improved and fewer experienced adverse effects, in comparison to our patients, because the patients had less advanced disease.

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ACCESSION NUMBER: 1986:96870 BIOSIS
DOCUMENT NUMBER: PREV198681007286; BA81:7286
TITLE: CLINICAL TRIAL OF PERGOLIDE IN PARKINSONS DISEASE.
AUTHOR(S): GONCE M [Reprint author]; DELWAIDE P J
CORPORATE SOURCE: SERV NEUROL-NEUROPHYSIOL CLIN, HOP BAVIERE, 4000, LIEGE,
BELGIQUE
SOURCE: Presse Medicale, (1985) Vol. 14, No. 26, pp.
1409-1411.
CODEN: PRMEEM. ISSN: 0755-4982.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: FRENCH
ENTRY DATE: Entered STN: 25 Apr 1986
Last Updated on STN: 25 Apr 1986

AB Pergolide is thought to stimulate both D1 and D2 dopaminergic receptors. Its effects on Parkinson's disease were evaluated in an open trial, using clinical assessment scales and objective tests. Nine patients had previously been treated with L-dopa, but the drug had either gradually lost its effectiveness or produced invalidating side-effects. Pergolide in doses of 2 mg per day considerably and durably improved the parkinsonian symptoms and enabled the patients to reduce L-dopa dosage by about 50%. Dyskinesia and « on-off » phenomena partially regressed. Significant improvement was also observed in 3 of 4 patients with Parkinson's disease who had no previously received L-dopa. The side-effects of pergolide were fairly frequent in both groups, but they were relatively mild and reversible.

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ACCESSION NUMBER: 1985175303 EMBASE
TITLE: Pergolide mesylate: Lack of cardiac toxicity in patients
with cardiac disease.
AUTHOR: Tanner, C.M.; Chhablani, R.; Goetz, C.G.; Klawans, H.L.
CORPORATE SOURCE: Department of Neurological Sciences, Rush-Presbyterian-St.
Luke's Medical Center, Chicago, IL 60612, United States.
SOURCE: Neurology, (1985) Vol. 35, No. 6, pp. 918-921.
ISSN: 0028-3878 CODEN: NEURAI
COUNTRY: United States

DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
020 Gerontology and Geriatrics
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery

LANGUAGE: English

ENTRY DATE: Entered STN: 10 Dec 1991

Last Updated on STN: 10 Dec 1991

AB In a 12-month open-label trial, pergolide mesylate was administered in doses with antiparkinsonian efficacy to six patients with stable heart disease. Cardiac status did not worsen in any patient. Parkinson's disease improved in all patients. Pergolide is a safe and effective therapy for Parkinson's disease, even in patients with heart disease.

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ACCESSION NUMBER: 1985167037 EMBASE

TITLE: Chronic agonist therapy for Parkinson's disease: A 5-year study of bromocriptine and pergolide.

AUTHOR: Goetz, C.G.; Tanner, C.M.; Glantz, R.H.; Klawans, H.L.

CORPORATE SOURCE: Department of Neurological Sciences, Rush-Presbyterian St. Luke's Medical Center, Chicago, IL 60612, United States.

SOURCE: Neurology, (1985) Vol. 35, No. 5, pp. 749-751.

ISSN: 0028-3878 CODEN: NEURAI

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 030 Clinical and Experimental Pharmacology

037 Drug Literature Index

008 Neurology and Neurosurgery

LANGUAGE: English

ENTRY DATE: Entered STN: 10 Dec 1991

Last Updated on STN: 10 Dec 1991

AB We used pergolide to treat 10 patients with idiopathic Parkinson's disease who had first responded to, and then failed, bromocriptine therapy. At the end of 5 years, patients had improved when compared with study entry. Peak efficacy, equal with both drugs, was seen at 12 months. After a mean treatment of 29 months, bromocriptine was no longer effective, but pergolide was still beneficial.

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ACCESSION NUMBER: 1985167034 EMBASE

TITLE: Long-term experience with pergolide therapy of advanced parkinsonism.

AUTHOR: Kurlan, R.; Miller, C.; Levy, R.; et. al.

CORPORATE SOURCE: Department of Neurology, University of Rochester Medical Center, Rochester, NY 14642, United States.

SOURCE: Neurology, (1985) Vol. 35, No. 5, pp. 738-742.

ISSN: 0028-3878 CODEN: NEURAI

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 030 Clinical and Experimental Pharmacology

037 Drug Literature Index

008 Neurology and Neurosurgery

LANGUAGE: English

ENTRY DATE: Entered STN: 10 Dec 1991

Last Updated on STN: 10 Dec 1991

AB Nine patients with idiopathic Parkinson's disease were treated with pergolide to a daily maintenance dose of 2.2 ± 0.9 mg (mean \pm SD) for 17.3 ± 8.3 months. After 1 month, there was an

average 68% increase in mobile on-time, but the improvement declined to 30% by 6 months, 23% by 1 year, and virtually disappeared by 18 months of therapy. Pergolide was discontinued in seven patients because of loss of efficacy (4 patients), confusion (1 patient), or myocardial infarction or ventricular ectopy (2 patients). Partial but temporary restoration of mobility was observed in seven patients who were switched to an alternate-day dosing schedule after 9.2 ± 2.4 months. Two patients with advanced Shy-Drager syndrome were treated with pergolide without benefit.

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ACCESSION NUMBER: 1985:338939 BIOSIS
DOCUMENT NUMBER: PREV198580008931; BA80:8931
TITLE: LONG-TERM STUDY OF PERGOLIDE IN PARKINSONS DISEASE.
AUTHOR(S): JANKOVIC J [Reprint author]
CORPORATE SOURCE: BAYLOR COLLEGE OF MEDICINE, DEPARTMENT OF NEUROLOGY, TEXAS
MEDICAL CENTER, HOUSTON, TEXAS 77030, USA
SOURCE: Neurology, (1985) Vol. 35, No. 3, pp. 296-299.
CODEN: NEURAI. ISSN: 0028-3878.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB In 18 patients with Parkinson's disease, the effects of pergolide after 28 mo. of treatment were compared with the response after the initial 10-wk therapy. At a mean 3.2-mg daily dose of pergolide, the daily dose of levodopa was still 33% lower than at the onset of pergolide therapy. The mean motor disability score, which decreased by 65% during the first 10 wk of pergolide, was still decreased by 42% after 28 mo. In the 12 patients with on-off effect, the percent time on increased 117% during the 1st phase of the study and was still increased 63% after more than 2 yr of pergolide therapy. Sudden freezing episodes became the most disabling problem in the majority of patients. Down regulation of dopamine receptors may contribute, but it is not the only cause of loss of responsiveness to pergolide.

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ACCESSION NUMBER: 1985:336761 BIOSIS
DOCUMENT NUMBER: PREV198580006753; BA80:6753
TITLE: DOUBLE-BLIND TRIAL OF PERGOLIDE FOR PARKINSONS DISEASE.
AUTHOR(S): DIAMOND S G [Reprint author]; MARKHAM C H; TRECIOKAS L J
CORPORATE SOURCE: UNIVERSITY OF CALIFORNIA, LOS ANGELES, DEPARTMENT OF
NEUROLOGY, REED NEUROLOGICAL RESEARCH CENTER, UCLA SCHOOL
OF MEDICINE, CENTER FOR THE HEALTH SCIENCES, LOS ANGELES,
CALIF 90024, USA
SOURCE: Neurology, (1985) Vol. 35, No. 3, pp. 291-295.
CODEN: NEURAI. ISSN: 0028-3878.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Pergolide mesylate, a dopamine agonist, was studied as adjunctive therapy in a 6-mo. double-blind trial in 20 patients with Parkinson's disease who were achieving less than optimal response from Sinemet. As pergolide or placebo was administered in increasing dosage. Sinemet was reduced if side effects developed. Both the pergolide and placebo groups improved significantly ($P < 0.05$). The pergolide group improved 30% at the end of 24 wk and the placebo group 23%. There was no significant difference between drug and placebo groups, possibly due to a fortuitous support group and the side effects that may have burdened the pergolide group.

Pergolide had a definite antiparkinsonian effect.

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ACCESSION NUMBER: 1985219421 EMBASE
TITLE: Pergolide therapy in Parkinson's disease: A double-blind, placebo-controlled study.
AUTHOR: Sage, J.I.; Duvoisin, R.C.
CORPORATE SOURCE: Department of Neurology, Rutgers Medical School, New Brunswick, NJ 08901, United States.
SOURCE: Clinical Neuropharmacology, (1985) Vol. 8, No. 3, pp. 260-265.
ISSN: 0362-5664 CODEN: CLNEDB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 020 Gerontology and Geriatrics
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 10 Dec 1991

AB A double-blind, placebo-controlled study was conducted of pergolide as an adjunctive treatment to levodopa in 17 patients with advanced Parkinson's disease. There was a significant improvement ($p < 0.05$) in total disability score, in gait, and in 'wearing off' and 'on-off' phenomena. Pergolide is a useful drug in patients with advanced Parkinson's disease.

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ACCESSION NUMBER: 1986022511 EMBASE
TITLE: New central dopamine agonists.
AUTHOR: Borsy, J.
CORPORATE SOURCE: Institute for Drug Research, H-1325 Budapest, Hungary.
SOURCE: Polish Journal of Pharmacology and Pharmacy, (1985) Vol. 37, No. 3, pp. 227-236.
ISSN: 0301-0244 CODEN: PJPPAA
COUNTRY: Poland
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 10 Dec 1991

AB Recently, the importance of the dopamine receptor agonists has increased in the treatment of parkinsonism, different endocrinological diseases and cardiovascular illness. In the therapy some well known drugs, derivatives of ergot groups e.g. bromocriptine, lisuride and pergolide, have been found useful. In the Institute for Drug Research numerous semi-synthetic elymoclavine derivatives were synthesized during the past years, and the influence of these new compounds on both the central and peripheral dopamine transmission was examined. Among the different ergot derivatives compound GYKI-32 887 seemed to be the most effective dopamine agonist and it was selected for preclinical investigation. The endocrinological effects and the pre- and postsynaptic dopamine receptor stimulant activity of this new compound are summarized. GYKI-32 887 was more potent than bromocriptine as regards its inhibitory effect on prolactin secretion and antiparkinsonian efficacy. Besides the strong dopamine receptor stimulant action this new ergoline

compound, contrary to bromocriptine, inhibits the convulsive action of bicucullin. It may be assumed that the GABA receptor agonistic effect of GYKI-32 887 would be also valuable in the treatment of various form of dyskinesias.

L9 ANSWER 288 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1985:106327 CAPLUS
DOCUMENT NUMBER: 102:106327
ORIGINAL REFERENCE NO.: 102:16567a,16570a
TITLE: Dopamine receptors: antiparkinsonian activity and molecular mechanisms
AUTHOR(S): Goldstein, Menek; Lew, Jow Y.; Lieberman, Abraham; Fuxe, Kjell
CORPORATE SOURCE: Sch. Med., New York Univ., New York, NY, USA
SOURCE: Aging 2000 [Two Thousand]: Our Health Care Destiny, [Proc. - Annu. Symp. Tex. Res. Inst. Ment. Sci.], 17th (1985), Meeting Date 1983, Volume 1, 147-54. Editor(s): Gaitz, Charles M.; Samorajski, Thaddeus. Springer: New York, N. Y. CODEN: 53BZAU
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 26 refs., on the antiparkinsonism activities of ergot derivs., including bromocriptine [25614-03-3], lergotrile [36945-03-6], and pergolide [66104-22-1], and on the characterization of solubilized striatal dopaminergic D2 receptors.

L9 ANSWER 289 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1985:516297 CAPLUS
DOCUMENT NUMBER: 103:116297
ORIGINAL REFERENCE NO.: 103:18475a,18476a
TITLE: Long-term use of dopamine agonists in Parkinson's disease
AUTHOR(S): Jankovic, Joseph
CORPORATE SOURCE: Texas Med. Cent., Baylor Coll. Med., Houston, TX, 77030, USA
SOURCE: Clinical Neuropharmacology (1985), 8(2), 131-40
CODEN: CLNEDB; ISSN: 0362-5664
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 51 refs. is given on the long-term use of bromocriptine [25614-03-3] and pergolide [66104-22-1] in the treatment of Parkinson's disease.
OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)

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ACCESSION NUMBER: 1986207330 EMBASE
TITLE: The use of pergolide and lisuride, two experimental dopamine agonists, in patients with advanced Parkinson disease.
AUTHOR: Lieberman, A.N.; Leibowitz, M.; Gopinathan, G.; et. al.
CORPORATE SOURCE: New York University School of Medicine, New York, NY, United States.
SOURCE: American Journal of the Medical Sciences, (1985) Vol. 290, No. 3, pp. 102-106. ISSN: 0002-9629 CODEN: AJMSA9
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index

038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 10 Dec 1991

AB Pergolide, an experimental dopamine agonist, was administered to 56 patients with advanced Parkinson disease who were no longer satisfactorily responding to levodopa, including 45 patients with diurnal oscillations in performance: 'on-off' phenomena. Lisuride, an experimental dopamine agonist was administered to 63 patients with advanced Parkinson disease. Pergolide or lisuride, when added to levodopa, resulted in a significant decrease in disability in both the 'on' and the 'off' period, and an increase in the number of hours in which patients were 'on'. Forty-one of 56 patients (73%) improved on Pergolide. Thirty-seven of 63 patients (59%) improved on lisuride. Mean dose of pergolide was 2.5 mg. (range 0.2 to 10.0 mg.). Mean dose of lisuride was 2.6 mg. (range 0.2 to 5.0 mg.). Pergolide was discontinued in 18 patients because of adverse effects, including an organic confusional syndrome (six patients), dyskinesias (four patients) and cardiovascular abnormalities (three patients). Lisuride was discontinued in 26 patients because of adverse effects, including an organic confusional syndrome (15 patients), dyskinesias (five patients) and vasospasm (two patients). Pergolide was discontinued in nine patients and lisuride in 12 because of a lack of effect or a declining effect. Both drugs are equally useful in patients with advanced Parkinson disease.

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ACCESSION NUMBER: 1985:1516 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 23-04130
TITLE: Drug abuse yields important clues to Parkinson's disease
AUTHOR(S): White, J. P.
SOURCE: Drug Topics (USA), (Sep 2 1985) Vol. 129, pp. 32-34.
CODEN: DRTOAJ. ISSN: 0012-6616.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 85:4459
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB Current information on the cause and treatment of Parkinson's disease is presented. Researchers found that 6 patients developed symptoms of the disease as a result of exposure to a chemical known as MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), an unwanted by-product of the illicit synthesis of a meperidine analog. Addicts either injected the substance repeatedly (as a heroin substitute) or accidentally assimilated it during synthesis. It was stated that Parkinson's disease can be specifically attributed to a deficit of dopamine and to a destruction or dysfunction of the nigrostriatal dopamine neurons in particular. Pargyline hydrochloride (Eutonyl), pergolide and domperidone (Motilium) are drugs being developed to both treat the disease and help retard its progress.
Elvira deC. Weiss

L9 ANSWER 292 OF 331 DISSABS COPYRIGHT (C) 2009 ProQuest Information and Learning Company; All Rights Reserved on STN

ACCESSION NUMBER: 84:18776 DISSABS Order Number: AAR8428452
TITLE: TIME DEPENDENT ALTERATIONS IN CENTRAL NERVOUS SYSTEM
DOPAMINE RECEPTORS INDUCED BY DOPAMINE AGONIST TREATMENT
AUTHOR: WILNER, KEITH DAVID [PH.D.]

CORPORATE SOURCE: THE UNIV. OF TEXAS H.S.C. AT HOUSTON GRAD. SCH. OF BIOMED.
SCI. (2034)
SOURCE: Dissertation Abstracts International, (1984) Vol.
45, No. 9B, p. 2881. Order No.: AAR8428452. 152 pages.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English
ENTRY DATE: Entered STN: 19921118
Last Updated on STN: 19921118

AB Levodopa, the precursor of dopamine, is currently the drug of choice in the treatment of Parkinson's disease. Recently, two direct dopamine agonists, bromocriptine and pergolide, have been tested for the treatment of Parkinson's disease because of reduced side effects compared to levodopa. Few studies have evaluated the effects of long-term treatment of dopamine agonists on dopamine receptor regulation in the central nervous system. Thus, the purpose of this study was to determine whether chronic dopamine agonist treatment produces a down-regulation of striatal dopamine receptor function and to compare the results of the two classes of dopaminergic drugs.

Levodopa with carbidopa, a peripheral decarboxylase inhibitor, was administered orally to rats whereas bromocriptine and pergolide were injected intraperitoneally once daily. Several neurochemical parameters were examined from 1 to 28 days.

Levodopa minimally decreased striatal D-1 receptor activity but increased the number of striatal D-2 binding sites. Levodopa increased the V(max) of tyrosine hydroxylase (TH) in all brain regions tested. Protein blot analysis of striatal TH indicated a significant increase in the amount of TH present. Dopamine-beta-hydroxylase (DBH) activity was markedly decreased in all brain regions studied and mixing experiments of control and drug-treated cortices did not show the presence of an increased level of endogenous inhibitors.

Bromocriptine treatment decreased the number of D-2 binding sites. Striatal TH activity was decreased and protein blot analysis indicated no change in TH quantity. The specificity of bromocriptine for striatal TH suggested that bromocriptine preferentially interacts with dopamine autoreceptors.

Combination levodopa-bromocriptine was administered for 12 days. There was a decrease in both D-1 receptor activity and D-2 binding sites, and a decrease in brain HVA levels suggesting a postsynaptic receptor action. Pergolide produced identical results to the combination levodopa-bromocriptine studies.

In conclusion, combination levodopa-bromocriptine and pergolide treatments exhibited the expected down-regulation of dopamine receptor activity. In contrast, levodopa appeared to up-regulate dopamine receptor activity. Thus, these data may help to explain, on a biochemical basis, the decrease in the levodopa-induced side effects noted with combination levodopa-bromocriptine or pergolide therapies in the treatment of Parkinson's disease.

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ACCESSION NUMBER: 1985:236131 BIOSIS
DOCUMENT NUMBER: PREV198579016127; BA79:16127
TITLE: CHRONIC L DOPA OR PERGOLIDE ADMINISTRATION INDUCES
DOWN-REGULATION OF DOPAMINE RECEPTORS IN DENERVATED
STRIATUM.
AUTHOR(S): RECHES A [Reprint author]; WAGNER H R; JACKSON-LEWIS V;
YABLONSKAYA-ALTER E; FAHN S
CORPORATE SOURCE: NEUROLOGICAL INST, 710 WEST 168TH ST, NEW YORK, NY 10032,
USA
SOURCE: Neurology, (1984) Vol. 34, No. 9, pp. 1208-1212.
CODEN: NEURAI. ISSN: 0028-3878.

DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Refractory response to dopamine (DA) agonists is a common problem in the treatment of Parkinson's disease. In rats with unilateral lesions of the substantia nigra, denervation induced significant increases in striatal 3(H)-spiperone binding sites ipsilateral to the lesion. Chronic treatment with levodopa or with with pergolide mesylate significantly decreased the number of 3(H)-spiperone striatal binding sites. Agonist-induced decreases were approximately equivalent in intact and denervated striata and did not appear to be affected by lesions. The poor response to DA agonist in certain parkinsonian patients with chronic drug exposure may be mediated by drug-induced DA receptor down-regulation.

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ACCESSION NUMBER: 1985127826 EMBASE
TITLE: The pharmacology of Parkinson's disease: Basic aspects and recent advances.
AUTHOR: Da Prada, M.; Keller, H.H.; Pieri, L.; et. al.
CORPORATE SOURCE: Pharmaceutical Research Department, F. Hoffmann-La Roche & Co., Ltd, CH-4002 Basel, Switzerland.
SOURCE: Experientia, (1984) Vol. 40, No. 11, pp. 1165-1172.
ISSN: 0014-4754 CODEN: EXPEAM
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 10 Dec 1991

AB Basic aspects and recent advances in the understanding of the pharmacological mechanism of action of the clinically most used antiparkinson drugs are reviewed. Recent human and animal biochemical investigations clearly confirm and extend previous findings indicating that benserazide is much more potent than carbidopa as peripheral decarboxylase inhibitor. L-DOPA in combination with benserazide or carbidopa constitutes the best available therapy for Parkinson's disease (PD). To reduce peaks and rapid fluctuations of L-DOPA plasma levels (possibly responsible for peak-dose dyskinesias and end-of-dose deterioration) a slow-release formulation of L-DOPA in combination with benserazide or with benserazide plus catechol-O-methyltransferase inhibitors should be developed. In parkinsonian patients under long-term L-DOPA therapy monoamine oxidase inhibitors type B (MAO-B) e.g. (-)deprenyl and direct dopamine receptor agonists (bromocriptine, lisuride, pergolide etc.), due to their L-DOPA-sparing effects, alleviate in some cases L-DOPA-induced side-effects e.g. dyskinesias and on-off phenomena. However, since (-)deprenyl, due to its metabolism to (-)methamphetamine and (-)amphetamine, seem to have indirect sympathomimetic activity, new selective MAO-B inhibitors devoid of indirect sympathomimetic effects should be tested clinically to assess the functional role of pure MAO-B inhibition in the therapy of PD. The auxiliary therapy with direct dopamine receptor agonists of the D-2 subtype represents another valid approach which should be further investigated in order to find novel dopamine agonists, less expensive than bromocriptine, and strictly selective for D-2 receptor sites.

L9 ANSWER 295 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1984:1507 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 22-04876
TITLE: Parkinson's disease in 1984: update
AUTHOR(S): Lang, A. E.; Blair, R. D. G.
CORPORATE SOURCE: 25 Leonard Ave., 205, Toronto, Ontario, Canada M5T 2R2
SOURCE: Canadian Medical Association Journal (Canada), (Nov 1 1984) Vol. 131, pp. 1031-1037. 71 Refs.
CODEN: CMAJAX. ISSN: 0008-4409.
DOCUMENT TYPE: General Review
FILE SEGMENT: IPA
OTHER SOURCE: IPA 84:5828
LANGUAGE: English
SUMMARY LANGUAGE: French
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB A review of important topics in the field of Parkinson disease, including etiologic studies, types and mechanisms of complications associated with levodopa therapy and their treatment, other treatment options, and when and how to begin treatment, is presented. The use of bromocriptine, lisuride, and pergolide, and the role of domperidone and monoamine oxidase inhibitors when used in combination with levodopa to improve therapy, are discussed.
Lilia M. Sancho

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ACCESSION NUMBER: 1984151420 EMBASE
TITLE: Pergolide in the treatment of Parkinson's disease.
AUTHOR: Mear, J.-Y.; Barroche, G.; De Smet, Y.; et. al.
CORPORATE SOURCE: Clinique de Neurologie et Neuropsychologie, Paris, France.
SOURCE: Neurology, (1984) Vol. 34, No. 7, pp. 983-986.
ISSN: 0028-3878 CODEN: NEURAI
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 020 Gerontology and Geriatrics
003 Endocrinology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 10 Dec 1991

AB Pergolide, a long-acting central dopamine agonist, was used as monotherapy in 16 parkinsonian patients. A mean daily dose of 6.3 mg resulted in 73% improvement of parkinsonian disability. Clinical improvement after acute administration of one dose of pergolide was similar to that observed after levodopa plus a peripheral decarboxylase inhibitor but at a dose 100 times lower (2.2 mg and 200 mg, respectively). The effect lasted twice as long (5 1/2 hours and 2 1/4 hours, respectively).

L9 ANSWER 297 OF 331 MEDLINE on STN DUPLICATE 226

ACCESSION NUMBER: 1984124663 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6695627
TITLE: Pergolide and lisuride in advanced Parkinson's disease.
AUTHOR: Lieberman A N; Gopinathan G; Neophytides A; Leibowitz M; Goldstein M
SOURCE: Advances in neurology, (1984) Vol. 40, pp. 503-7.
Journal code: 0367524. ISSN: 0091-3952.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198403
ENTRY DATE: Entered STN: 19 Mar 1990
Last Updated on STN: 19 Mar 1990
Entered Medline: 7 Mar 1984

AB In a retrospective study, treatment with lisuride was compared to pergolide in 25 patients with advanced PD in whom the response to levodopa had diminished. Sixteen patients had wearing off and/or ON-OFF phenomena. Lisuride or pergolide, when added to levodopa, resulted in comparable and significant decreases in disability in both ON and OFF periods; pergolide resulted in a greater increase in the number of hours in which patients were ON. Adverse reactions were comparable on both drugs. However, patients who developed an adverse reaction on one drug did not necessarily develop the same reaction on the other drug. Both lisuride and pergolide are effective anti-Parkinson drugs.

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ACCESSION NUMBER: 1984:358160 BIOSIS
DOCUMENT NUMBER: PREV198478094640; BA78:94640
TITLE: THE BEHAVIORAL PHARMACOLOGY OF AY-27110 S LEVO-2-4-2
HYDROXY-2-3' 4'-DIMETHOXYPHENYLETHYL-1-PIPERAZINYL-2 4 6
CYCLO HEPTATRIEN-1-ONE A NOVEL NONERGOT DOPAMINERGIC
AGONIST.
AUTHOR(S): VOITH K [Reprint author]
CORPORATE SOURCE: DEP PHARMACOL, AYERST LAB RES, INC, CN 8000, PRINCETON, NJ
08540, USA
SOURCE: Drug Development Research, (1984) Vol. 4, No. 4,
pp. 391-404.
CODEN: DDREDK. ISSN: 0272-4391.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB AY-27,110 is the pharmacologically active enantiomer of a troponylpiperazine derivative. At low doses, the compound induced contralateral rotation behavior in rats with a unilateral 6-OHDA [6-hydroxydopamine] lesion of the nigrostriatal pathway, at higher doses it caused weak stereotypy and in dogs it elicited emesis. The actions of AY-27,110 were dose-dependently antagonized by haloperidol and pimozide, but were not diminished by α -MPT [α -methyl-p-tyrosine] or reserpine pretreatment. Evidently AY-27,110 is a chemically novel dopaminergic agonist that should be useful as an anti-parkinson drug. Since the effects of AY-27,110 are independent of intact catecholamine synthesis and storage mechanisms, the compound should be efficacious in patients with advanced Parkinson's disease. AY-27,110 was compared to several ergot-derived dopamine agonists, namely bromocriptine, lisuride and pergolide, to predict its potency, side-effect liability and potential therapeutic advantages.

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ACCESSION NUMBER: 1984060320 EMBASE
TITLE: Long-term treatment with pergolide: Decreased efficacy with
time.
AUTHOR: Lieberman, A.N.; Goldstein, M.; Leibowitz, M.; et. al.
CORPORATE SOURCE: New York University School of Medicine, New York, NY,
United States.
SOURCE: Neurology, (1984) Vol. 34, No. 2, pp. 223-226.
ISSN: 0028-3878 CODEN: NEURAI

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 020 Gerontology and Geriatrics
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery

LANGUAGE: English

ENTRY DATE: Entered STN: 10 Dec 1991

Last Updated on STN: 10 Dec 1991

AB We studied the effect of pergolide (combined with levodopa) in 17 patients with Parkinson's disease, including 15 with 'wearing off' or on-off phenomena, who had been taking pergolide for at least 2 years. Mean duration of the study was 27.8 months. All 17 patients improved initially, but the improvement later faded. Mean disability score, which decreased initially by 60% (significant), was decreased only by 20% after 2 years (not significant). Wearing off and on-off phenomena, which improved initially, became prominent again. Four patients lost all the improvement, nine patients lost much of the improvement, and four maintained much of the improvement. Mean dose of pergolide was 2.2 mg (range, 0.8 to 5.0 mg).

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ACCESSION NUMBER: 1984060313 EMBASE

TITLE: Pergolide therapy for Parkinson's disease: Neurobehavioral changes.

AUTHOR: Stern, Y.; Mayeux, R.; Ilson, J.; et. al.

CORPORATE SOURCE: Department of Neurology, Columbia University College of Physicians and Surgeons, New York, NY 10032, United States.

SOURCE: Neurology, (1984) Vol. 34, No. 2, pp. 201-204.

ISSN: 0028-3878 CODEN: NEURAI

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 020 Gerontology and Geriatrics
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery

LANGUAGE: English

ENTRY DATE: Entered STN: 10 Dec 1991

Last Updated on STN: 10 Dec 1991

AB Pergolide mesylate, a long-acting dopamine agonist, is effective in treating Parkinson's disease. Behavioral change is said to be one adverse effect. We therefore studied 19 parkinsonian patients with neuropsychological tests before and after initiating pergolide therapy. Intellectual and behavioral changes were also monitored clinically for up to 2 years. There was no decline in performance on the neuropsychological tests. Six patients had transient psychiatric or intellectual changes that were controlled by reducing drug dosage. These changes were similar to those seen with other dopamine agonists.

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ACCESSION NUMBER: 1984109549 EMBASE

TITLE: Suppression of REM rebound by Pergolide.

AUTHOR: Askenasy, J.J.M.; Yahr, M.D.

CORPORATE SOURCE: Mount Sinai School of Medicine, Department of Neurology, New York, NY, United States.

SOURCE: Journal of Neural Transmission - General Section, (1984) Vol. 59, No. 2, pp. 151-159.

CODEN: JNTMAH
COUNTRY: Austria
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery

LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 10 Dec 1991

AB A 71 year old retired printer developed idiopathic Parkinson's disease over a period of 3 years. On account of his worsening condition he was admitted to hospital. Following the interruption of his medication the patient developed an akinetic crisis. A 48 hour polysomnogram recording, repeated five times during hospitalization, showed severe sleep deprivation. Treatment with Pergolide alone was then started; and sleep monitoring showed suppression of REM rebound, REM only appearing when the dose of the drug was reduced. It is suggested that REM rebound phenomena produced by sleep deprivation in a Parkinson's disease patient are suppressed by the effect of the dopaminergic agent Pergolide.

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STN DUPLICATE 231

ACCESSION NUMBER: 1985:236136 BIOSIS
DOCUMENT NUMBER: PREV198579016132; BA79:16132
TITLE: PERGOLIDE THERAPY IN PARKINSONS DISEASE.
AUTHOR(S): JEANTY P [Reprint author]; VAN DEN KERCHOVE M; LOWENTHAL A;
DE BRUYNE H
CORPORATE SOURCE: UNIVERSITAIRE INSTELLING ANTWERPEN, LABORATORY OF
NEUROCHEMISTRY, B-2610 ANTWERP, BELGIUM
SOURCE: Journal of Neurology, (1984) Vol. 231, No. 3, pp.
148-152.
CODEN: JNRYA9. ISSN: 0340-5354.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB A total of 26 patients were treated with pergolide mesylate, a semi-synthetic ergot derivative with the property of direct dopamine activity. Of these patients, 18 suffered from late failure of L-dopa, while the remaining 8 had never before been treated with L-dopa. The activity of pergolide was studied, either by giving it to untreated patients or by reducing as much as possible the L-dopa given in patients with parkinsonism. Adverse effects and failure rate were reduced by slowly increasing the daily dosage, by giving considerable dose flexibility whenever side effects were manifest, and by the use of relatively low doses (mean of 3.8 mg in the L-dopa-group and 2.9 in the other group). From 26 patients, 13 (50%) still remain in the study for an average treatment period of 16 mo. (3 wk to 25 mo. for the groups as a whole). All patients experienced a beneficial effect from pergolide, especially during the 1 months of treatment, in self-care, rigidity, gait and automatic movements. Slight or no improvement was seen in tremor, speech and posture. The most frequent side effects were nausea and vomiting (in the initial phase of the treatment), insomnia and psychotoxic reactions (mostly periods of confusion accompanied by visual hallucinations and paranoid illusions). Pergolide mesylate is a useful additive for treatment of parkinsonism, but special attention should be paid to the important psychotoxic adverse effects that may appear, even at a low dose.

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ACCESSION NUMBER: 1984161180 EMBASE

TITLE: Erythromelalgia following pergolide administration.
AUTHOR: Monk, B.E.; Parkes, J.D.; Du Vivier, A.
CORPORATE SOURCE: Department of Dermatology, King's College Hospital, London SE5, United Kingdom.
SOURCE: British Journal of Dermatology, (1984) Vol. 111, No. 1, pp. 97-99.
ISSN: 0007-0963 CODEN: BJDEAZ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
052 Toxicology
005 General Pathology and Pathological Anatomy
038 Adverse Reactions Titles
037 Drug Literature Index
030 Clinical and Experimental Pharmacology
013 Dermatology and Venereology
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 10 Dec 1991

AB Two patients are described in whom treatment of Parkinson's disease with the ergot derivative pergolide was associated with the development of erythromelalgia. The possible mechanism of pergolide-induced erythromelalgia is briefly discussed.

L9 ANSWER 304 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1984:680 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 22-00989
TITLE: Erythromelalgia following pergolide administration
AUTHOR(S): Monk, B. E.; Parkes, J. D.; Du Vivier, A.
CORPORATE SOURCE: Dept. of Dermatology and Neurology, King's College Hosp., London SE5, England
SOURCE: British Journal of Dermatology (England), (Jul 1984) Vol. 3, pp. 97-99. 9 Refs.
CODEN: BJDEAZ. ISSN: 0007-0963.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 84:2453
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB Two patients (aged 67 and 68 yr) with Parkinson's disease developed erythromelalgia after many months of treatment with pergolide. Both patients gained so much benefit from I in terms of symptomatic relief of Parkinson's disease that the drug was not discontinued.
Elvira deC. Weiss

L9 ANSWER 305 OF 331 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN DUPLICATE 233
ACCESSION NUMBER: 1983209049 EMBASE
TITLE: Evaluating the evaluations: Or how to weigh the scales of parkinsonian disability.
AUTHOR: Diamond, S.G.; Markham, C.H.
CORPORATE SOURCE: Dep. Neurol., UCLA Sch. Med., Los Angeles, CA 90024, United States.
SOURCE: Neurology, (1983) Vol. 33, No. 8, pp. 1098-1099.
ISSN: 0028-3878 CODEN: NEURAI
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 020 Gerontology and Geriatrics
008 Neurology and Neurosurgery

LANGUAGE: English
ENTRY DATE: Entered STN: 9 Dec 1991
Last Updated on STN: 9 Dec 1991

AB We used four disability scales to evaluate eight patients with Parkinson's disease who were treated with pergolide mesylate for 1 year. Disability was rated on all four scales by the same neurologist at each of 11 visits. Prior ratings were not available to the examiner, who did not know that the scales themselves were an object of study. Disability scores, converted to percentage improvement relative to baseline, varied considerably between scales; for instance, at 5 months, one showed 13% improvement and another 58%. At 9 months, one showed worsening of 6% and another showed improvement of 34%. The four disability scales clearly measure different aspects of parkinsonism, and comparing results of different studies may not be valid if the disability scales are not the same.

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STN DUPLICATE 234

ACCESSION NUMBER: 1984:197109 BIOSIS
DOCUMENT NUMBER: PREV198477030093; BA77:30093
TITLE: COMPARISON OF PERGOLIDE AND BROMOCRIPTINE THERAPY IN
PARKINSONISM.
AUTHOR(S): LEWITT P A [Reprint author]; WARD C D; LARSEN T A;
RAPHAELSON M I; NEWMAN R P; FOSTER N; DAMBROSIA J M; CALNE
D B
CORPORATE SOURCE: BUILD 10, ROOM 5C101, NATL INST HEALTH, BETHESDA, MD 20205,
USA
SOURCE: Neurology, (1983) Vol. 33, No. 8, pp. 1009-1014.
CODEN: NEURAI. ISSN: 0028-3878.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Parkisonian patients (24) compared pergolide and bromocriptine therapy in a randomized double-blind, 2-period crossover study. Both drugs were adjusted to an optimal balance between benefits and side effects. The mean daily dose and dose range for pergolide and bromocriptine were 3.3 mg (0.7-7.2) and 42.7 mg (5.8-87.5), respectively. Adjunctive medications, which for most patients included levodopa (plus carbidopa), were not altered during the study. A similar spectrum of clinical effects was found with both drugs and with lisuride, which was used to treat 13 of the patients in a previous study. Despite neurochemical differences in the antiparkinsonian ergots, their clinical utility is quite similar. Hepatotoxicity and pleural reactions may occur rarely with these drugs.

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STN DUPLICATE 235

ACCESSION NUMBER: 1984:261288 BIOSIS
DOCUMENT NUMBER: PREV198477094272; BA77:94272
TITLE: PERGOLIDE IN PARKINSONS DISEASE.
AUTHOR(S): GOETZ C G [Reprint author]; TANNER C M; GLANTZ R; KLAWANS H
L
CORPORATE SOURCE: DEP NEUROL SCI, RUSH-PRESBYTERIAN ST LUKE'S MED CENT,
CHICAGO REPRINTS NOT AVAILABLE
SOURCE: Archives of Neurology, (1983) Vol. 40, No. 13,
pp. 785-787.
CODEN: ARNEAS. ISSN: 0003-9942.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Patients (22) received pergolide mesylate for Parkinson's disease for 1 yr. Improvement was maximal at 6 mo., but average

functional scores were still better at 12 mo., than at pretreatment evaluation. On-off fluctuations were reduced in severity, and 2 of 18 patients experienced full resolutions. Pergolide is an effective and safe ongoing medication for Parkinson's disease.

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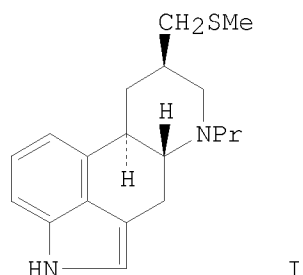
ACCESSION NUMBER: 1984:221194 BIOSIS
DOCUMENT NUMBER: PREV198477054178; BA77:54178
TITLE: MICROBIAL TRANSFORMATIONS OF PERGOLIDE TO PERGOLIDE SULFOXIDE AND PERGOLIDE SULFONE.
AUTHOR(S): SMITH R V [Reprint author]; DAVIS P J; KERR K M
CORPORATE SOURCE: DRUG DYNAMICS INSTITUTE, COLL PHARMACY, UNIV TEXAS AUSTIN, AUSTIN, TEX 78712, USA
SOURCE: Journal of Pharmaceutical Sciences, (1983) Vol. 72, No. 7, pp. 733-736.
CODEN: JPMSAE. ISSN: 0022-3549.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Using the rationale of 'microbial models of mammalian metabolism', a study was undertaken to identify microorganisms which form the 2 metabolites found in mammalian species. Fifty-eight microorganisms were investigated for their ability to effect the biotransformation of the ergoline alkaloid pergolide [used to treat hyperprolactinemia and Parkinson's disease]. A majority of these organisms formed pergolide sulfoxide, and a *Helminthosporium* species was investigated in greater detail since it yielded significant amounts of pergolide sulfoxide. A preparative-scale transformation afforded material which was identified as the sulfoxide based on melting point, spectral, and chromatographic comparison with authentic material as well as its conversion to pergolide by reduction with triphenylphosphine. An analytical high-performance liquid chromatographic determination of the enzymatic vs. spontaneous air-oxidation of pergolide in growing cultures and controls showed negligible air-oxidation and an .apprx. 40% enzymatic conversion of pergolide to the sulfoxide. Several organisms, including *Aspergillus alliaceus* formed a second metabolite, pergolide sulfone, which was identified on the basis of co-chromatographic data.

L9 ANSWER 309 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1983:551937 CAPLUS
DOCUMENT NUMBER: 99:151937
ORIGINAL REFERENCE NO.: 99:23143a,23146a
TITLE: Long lasting action of the dopamine receptor agonist pergolide on locomotor activity in rats
AUTHOR(S): De Marino, V.; Basile, V.; Amoroso, S.; Annunziato, L.
CORPORATE SOURCE: Dep. Pharmacol., II Fac. Med., Naples, 80131, Italy
SOURCE: IRCS Medical Science: Library Compendium (1983), 11(7), 621-2
CODEN: IRLCDZ; ISSN: 0305-6651
DOCUMENT TYPE: Journal
LANGUAGE: English

GI



AB Pergolide (I) [66104-22-1] (0.1-3 mg/kg, s.c.) induced a dose-related, long-lasting stimulation of locomotor activity in rats, with a maximal increase of 600% observed at 3 mg/kg after 1 h. This effect was antagonized by penfluridol administered 12 h before I. Thus, I actions are probably mediated via dopaminergic receptors, and therefore, I may be useful clin. in the treatment of on-off phenomema which occurs during long term L-DOPA [59-92-7] therapy of Parkinsonism.

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ACCESSION NUMBER: 1983118184 EMBASE
 TITLE: Controlled trial of pergolide mesylate in Parkinson's disease and progressive supranuclear palsy.
 AUTHOR: Jankovic, J.
 CORPORATE SOURCE: Dep. Neurol., Baylor Coll. Med., Texas Med. Cent., Houston, TX 77030, United States.
 SOURCE: Neurology, (1983) Vol. 33, No. 4, pp. 505-507.
 ISSN: 0028-3878 CODEN: NEURAI
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 037 Drug Literature Index
 038 Adverse Reactions Titles
 008 Neurology and Neurosurgery
 LANGUAGE: English
 ENTRY DATE: Entered STN: 9 Dec 1991
 Last Updated on STN: 9 Dec 1991

AB We evaluated pergolide in 22 patients with Parkinson's disease and 3 with progressive supranuclear palsy (PSP). After achieving an optimal dose of pergolide and Sinemet, a matching placebo was substituted in double-blind manner. The mean dose of levodopa (in Sinemet) was reduced by 68%; in eight patients, pergolide completely replaced levodopa. In parkinsonian patients, the mean Hoehn-Yahr stage decreased from 3.2 to 1.6, and the mean total disability score decreased from 48.3 to 17.8. In 10 patients with on-off phenomenon, the time on increased 174% with pergolide. There was little effect in PSP. Postural light-headedness and reversible mental changes were seen.

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ACCESSION NUMBER: 1983:278112 BIOSIS
 DOCUMENT NUMBER: PREV198376035604; BA76:35604
 TITLE: PROGRESSIVE SUPRANUCLEAR PALSY CLINICAL FEATURES AND RESPONSE TO TREATMENT IN 16 PATIENTS.
 AUTHOR(S): JACKSON J A [Reprint author]; JANKOVIC J; FORD J
 CORPORATE SOURCE: DEP NEUROLOGY, BAYLOR MED, TEX MED CENTER, HOUSTON, TEX 77030, USA
 SOURCE: Annals of Neurology, (1983) Vol. 13, No. 3, pp.

273-278.

CODEN: ANNED3. ISSN: 0364-5134.

DOCUMENT TYPE: Article

FILE SEGMENT: BA

LANGUAGE: ENGLISH

AB Among 415 patients with parkinsonism, 16 (3.9%) had findings of progressive supranuclear palsy (PSP). This report reviews the clinical features and response to drug therapy in those 16 patients. Anticholinergic drugs failed to benefit any of the 5 patients treated, while presynaptic dopaminergic drugs (Sinemet or amantadine) were beneficial in only 5 of 22 patient trials. Alternatively, dopamine agonists (bromocriptine and pergolide) caused improvement in 9 of 14 patient trials, despite the fact that all but 1 of these patients had previously failed to respond to presynaptic dopaminergic drugs. Dopamine agonists such as bromocriptine and pergolide may be useful in some patients with PSP.

L9 ANSWER 312 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 238

ACCESSION NUMBER: 1983:605969 CAPLUS

DOCUMENT NUMBER: 99:205969

ORIGINAL REFERENCE NO.: 99:31532h,31533a

TITLE: Therapeutic potentials of centrally acting dopamine and α 2-adrenoreceptor agonists

AUTHOR(S): Goldstein, M.; Engel, J.; Lieberman, A.; Regev, I.; Bystritsky, A.; Mino, S.

CORPORATE SOURCE: Med. Cent., New York Univ., New York, NY, 10016, USA

SOURCE: Journal of Neural Transmission, Supplement (1983), 18(Basic Aspects Recept. Biochem.), 257-63

CODEN: JNTSD4; ISSN: 0303-6995

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The semisynthetic ergoline pergolide [66104-22-1], the partial ergoline LY 141865 [80373-22-4], and the 8- α -aminoergoline CU 32-085 [72786-12-0] were effective antitremor agents in monkeys with ventromedial tegmental lesions. The administration of pergolide or LY 141865 results in a relief of tremor with a concomitant occurrence of severe abnormal involuntary movements, whereas the administration of CU 32-085 results in a relief of tremor with the occurrence of only minor abnormal involuntary movements. Clin. studies revealed that pergolide is an effective drug in patients with advanced Parkinson's disease, and it reduces the on-off phenomena. The possible regulation of dopamine [51-61-6] neurotransmission by the norepinephrine [51-41-2] neuronal systems was reviewed. Preliminary data suggest that clonidine [4205-90-7] may interact with presynaptic dopamine receptors.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L9 ANSWER 313 OF 331 MEDLINE on STN DUPLICATE 239

ACCESSION NUMBER: 1983227592 MEDLINE

DOCUMENT NUMBER: PubMed ID: 6858770

TITLE: The effects of pergolide on the cardiovascular system of 40 patients with Parkinson's disease.

AUTHOR: Leibowitz M; Lieberman A N; Neophytides A; Gopinathan G; Goldstein M

SOURCE: Advances in neurology, (1983) Vol. 37, pp. 121-30.

Journal code: 0367524. ISSN: 0091-3952.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 198307
ENTRY DATE: Entered STN: 19 Mar 1990
Last Updated on STN: 19 Mar 1990
Entered Medline: 8 Jul 1983

AB The effect of pergolide, a semisynthetic ergot alkaloid, on the cardiovascular system of 40 patients with Parkinson's disease (PD) was evaluated. The mean daily dose of pergolide was 2.4 mg (range, 0.1 to 10 mg). The mean duration of follow-up was 6 months (range, 2 weeks to 20 months). The 40 patients were selected only on the basis of severe PD. All 13 patients in the first part of the study underwent 1 to 5 days of Holter monitoring before starting pergolide. Monitoring was then carried out for an additional period of between 2 and 10 weeks while the patients were on pergolide. Seven of the 13 patients manifested repetitive ventricular rhythms. These were isolated and unassociated with increases in premature ventricular contractions. The dose at which the RVRs occurred was a function of the presence or absence of heart disease. The changes occurred below 3 mg/day in patients with heart disease and above 3 mg/day in patients without heart disease. Pergolide was discontinued in three of the patients with heart disease. It was concluded that pergolide may, in the diseased heart, predispose to RVRs. In the second part of the study, Holter monitoring was carried out only at the discretion of the cardiologist, and five patients were so monitored. None of these patients was rejected from the study. Only one patient (with heart disease) of the 27 patients in the second part of the study experienced an arrhythmia. This consisted of an increase in PVCs on 4 mg/day of pergolide. Pergolide was discontinued. Eight of the 40 patients in these early dose-ranging studies experienced orthostasis, two with syncope, immediately on addition of pergolide (0.1 to 0.4 mg) to levodopa. The orthostasis could be eliminated in all but two patients by reducing or discontinuing levodopa.

L9 ANSWER 314 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
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ACCESSION NUMBER: 1983:317468 BIOSIS
DOCUMENT NUMBER: PREV198376074960; BA76:74960
TITLE: PERGOLIDE INDUCED CIRCLING IN RATS WITH 6 HYDROXY DOPAMINE
LESIONS IN THE NIGRO STRIATAL PATHWAY.
AUTHOR(S): DUVOISIN R C [Reprint author]; HEIKKILA R E; MANZINO L
CORPORATE SOURCE: DEP NEUROL, UMDNJ-RUTGERS MED SCH, PO BOX 101, PISCATAWAY,
NJ 08854, USA
SOURCE: Neurology, (1982) Vol. 32, No. 12, pp. 1387-1391.
CODEN: NEURAI. ISSN: 0028-3878.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB In rats with a unilateral 6-hydroxydopamine lesion of the nigrostriatal system the behavioral effects of pergolide were compared with those of L-dopa, bromocriptine and lergotrile. In this animal model of parkinsonism, doses of 0.25 mg/kg pergolide (free base) induced vigorous circling for 24 h. Pergolide was more potent than bromocriptine or lergotrile. Pretreatment with α -methyl-p-tyrosine nearly abolished the effects of bromocriptine, markedly diminished the effects of lergotrile and only partially diminished the effects of pergolide. Apparently, pergolide should be more effective than bromocriptine in the treatment of parkinsonism.

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ACCESSION NUMBER: 1983:247933 BIOSIS

DOCUMENT NUMBER: PREV198376005425; BA76:5425
TITLE: FURTHER STUDIES WITH PERGOLIDE IN PARKINSON DISEASE.
AUTHOR(S): LIEBERMAN A N [Reprint author]; GOLDSTEIN M; GOPINATHAN G;
LEIBOWITZ M; NEOPHYTIDES A; WALKER R; HIESIGER E; NELSON J
CORPORATE SOURCE: 530 FIRST AVE, SUITE 5A, NEW YORK, NY 10016, USA
SOURCE: Neurology, (1982) Vol. 32, No. 10, pp. 1181-1184.
CODEN: NEURAI. ISSN: 0028-3878.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Pergolide was administered to 56 patients with advanced Parkinson disease who were no longer satisfactorily responding to levodopa. The group included 45 patients with on-off phenomena. Pergolide, when combined with levodopa, resulted in a 44% decrease in disability as assessed in the on period, a 15% decrease in disability in the off period and a 148% increase in the number of hours in which patients were on (from 4.6 ± 0.3 to 11.4 ± 0.6 h). All these changes were significant at 1%. Of the 56 patients, 41 (59%) improved when pergolide was added to levodopa. Mean dose of pergolide was 2.5 mg (range, 0.2-10.0 mg). Mean duration of the study was 13 mo. (range, 1 day to 34 mo.). Maximum improvement occurred within 2 mo. and began to decline, usually after 6 mo. The major adverse effects necessitating discontinuing pergolide were the occurrence of an organic confusional syndrome (6 patients), increased dyskinesias (4 patients) and cardiovascular abnormalities (3 patients). Nine patients discontinued pergolide because of a lack of effect or declining effect.

L9 ANSWER 316 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 242

ACCESSION NUMBER: 1983:247932 BIOSIS
DOCUMENT NUMBER: PREV198376005424; BA76:5424
TITLE: PERGOLIDE MESYLATE AND IDIOPATHIC PARKINSON DISEASE.
AUTHOR(S): TANNER C M [Reprint author]; GOETZ C G; GLANTZ R H; GLATT S L; KLAWANS H L
CORPORATE SOURCE: DEP NEUROLOGICAL SCI, RUSH-PRESBYTERIAN-ST LUKE'S MED CENT, 1725 W HARRISON, CHICAGO, ILL 60612, USA
SOURCE: Neurology, (1982) Vol. 32, No. 10, pp. 1175-1179.
CODEN: NEURAI. ISSN: 0028-3878.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The effects of pergolide mesylate were studied in an open trial of 23 patients with idiopathic Parkinson disease (PD). All had suffered from loss of efficacy or dose-limiting side effects on current antiparkinsonian regimens. On pergolide therapy, improvement, which was maintained for 6 mo., was noted in some parkinsonian features in all 23 patients. All patients suffering from on-off phenomenon were helped by pergolide. Significant side effects were not encountered. Pergolide is useful in the treatment of PD.

L9 ANSWER 317 OF 331 TOXCENTER COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1982:1401 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 20-05654
TITLE: Cholinergic and dopaminergic mechanisms in Parkinson's disease after long term levodopa administration
AUTHOR(S): Yahr, M. D.; Clough, C. G.; Bergmann, K. J.
CORPORATE SOURCE: Clin. Ctr. for Res. in Parkinson's and Allied Disorders, Mt. Sinai School of Med., New York, NY 10029
SOURCE: Lancet (England), (Sep 25 1982) Vol. 2, pp.

709-710. 3 Refs.

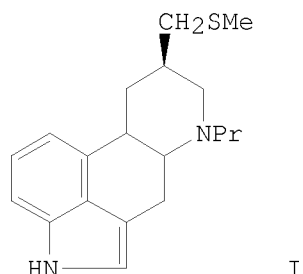
CODEN: LANCAO. ISSN: 0023-7507.

DOCUMENT TYPE: Letter
FILE SEGMENT: IPA
OTHER SOURCE: IPA 82:4830
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB The cholinergic and dopaminergic mechanisms in Parkinson disease were investigated in 19 patients who developed fluctuating therapy responses during long term therapy with Sinemet (I; carbidopa, combination, levodopa) alone (7 patients) and I plus bromocriptine or pergolide (14 patients). Results showed random fluctuations during the on-off and end-start dose. A return of cholinergic supersensitivity and of denervation supersensitivity reactive to endogenous fluctuating levels of acetylcholine following long term levodopa administration is suggested.
Lilia M. Sancho

L9 ANSWER 318 OF 331 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 243

ACCESSION NUMBER: 1983:65337 CAPLUS
DOCUMENT NUMBER: 98:65337
ORIGINAL REFERENCE NO.: 98:9861a,9864a
TITLE: Degree of selectivity of pergolide as an agonist at presynaptic versus postsynaptic dopamine receptors: implications for prevention or treatment of tardive dyskinesia
AUTHOR(S): Fuller, Ray W.; Clemens, James A.; Hynes, Martin D., III
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Journal of Clinical Psychopharmacology (1982), 2(6), 371-5
CODEN: JCPYDR; ISSN: 0271-0749
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB pergolide (I) [66104-22-1] is a potent dopamine [51-61-6] agonist that is being evaluated clin. in Parkinson's disease, hyperprolactinemia, and other diseases. I activates both presynaptic and postsynaptic dopamine receptors, with some apparent selectivity for the presynaptic dopamine autoreceptors. In rats, low doses of I mesylate (≤ 0.01 mg/kg, i.p.) decreased dopamine turnover in brain, decreased serum prolactin [9002-62-4] concentration, and reduced blood pressure in spontaneously hypertensive rats. At somewhat higher doses (≥ 0.05

mg/kg, i.p.), I caused contralateral turning in nigrostriatal-lesioned rats, elevation of serum corticosterone [50-22-6], and hypermotility with stereotyped behavior. All of these actions appear to be due to stimulation of dopamine receptors at various sites, but I may have preferential affinity for presynaptic dopamine receptors. If low doses of I can reduce dopaminergic transmission by activating presynaptic receptors that control dopamine release, then this action might be therapeutically useful in treating schizophrenia without causing tardive dyskinesia or in the treatment of tardive dyskinesia.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L9 ANSWER 319 OF 331 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 244

ACCESSION NUMBER: 1983:224745 BIOSIS
DOCUMENT NUMBER: PREV198375074745; BA75:74745
TITLE: LOCO MOTOR HYPO KINESIA IN THE RESERPINE TREATED RAT DRUG EFFECTS FROM THE CORPUS STRIATUM AND NUCLEUS ACCUMBENS.
AUTHOR(S): JOHNELS B [Reprint author]
CORPORATE SOURCE: DEP OF NEUROL, UNIV OF GOTEBOG, GOTEBOG, SWEDEN
SOURCE: Pharmacology Biochemistry and Behavior, (1982) Vol. 17, No. 2, pp. 283-290. CODEN: PBBHAU. ISSN: 0091-3057.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB A mechanographic method was used to assess the locomotor performance induced by apomorphine or other dopaminergic drugs in reserpine-treated rats. Reserpine induced locomotor hypokinesia. The hypokinesia was dose-dependently reversed by apomorphine (APO), bromocriptine and pergolide. Locomotion was induced by microinjection of APO into the nucleus accumbens. No locomotor effect was found after injection into corpus striatum. Injection into both nuclei was not superior to accumbens only. Intra-striatal or intraaccumbens injections of trifluoperazine blocked the effect on locomotion by systematic apomorphine. Evidently reserpine-induced locomotor hypokinesia is reversed by dopaminergic stimulation in the nucleus accumbens. Blockade of striatal or accumbens' dopamine receptors may counteract apomorphine-induced locomotion, presumably by interaction with postural motor control. Evidence was found for separate dopaminergic control of locomotion and muscle tone. This may be of importance for the development of new antiparkinson drugs.

=> S selegiline/ab and (parkinson? or antiparkinson?)/ab

'AB' IS NOT A VALID FIELD CODE

0 SELEGILINE/AB
0 PARKINSON?/AB
0 ANTIPARKINSON?/AB

L12 0 SELEGILINE/AB AND (PARKINSON? OR ANTIPARKINSON?)/AB

=> FILE MEDICINE

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COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.28	1272.45

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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[illegible]

=> S L13 and (parkinson? or antiparkinson?)/ab

[illegible]

=> S L14 and pd<2003

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'2003' NOT A VALID FIELD CODE
'2003' NOT A VALID FIELD CODE
'2003' NOT A VALID FIELD CODE
  16 FILES SEARCHED...
'2003' NOT A VALID FIELD CODE
  22 FILES SEARCHED...
'2003' NOT A VALID FIELD CODE
'2003' NOT A VALID FIELD CODE
  30 FILES SEARCHED...
  34 FILES SEARCHED...
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=> DUP REM L15

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PROCESSING COMPLETED FOR L15

=> S L16 and pergolide

=> D L17 1-76 IBIB ABS

DOCUMENT NUMBER: PREV200200260796
TITLE: Rapid-eye-movement sleep disorders in Parkinson's disease.
Original Title: Les troubles du sommeil paradoxal dans la
maladie de Parkinson.
AUTHOR(S): Gagnon, J.-F.; Montplaisir, J.; Bedard, M.-A. [Reprint
author]
CORPORATE SOURCE: Unite des Troubles du Mouvement Andre Barbeau, Hotel-Dieu,
CHUM, 3840, rue St-Urbain, Montreal, Quebec, H2W 1T8,
Canada
bedard.marc-andre@uqam.ca
SOURCE: Revue Neurologique (Paris), (Fevrier, 2002) Vol.
158, No. 2, pp. 135-152. print.
CODEN: RENEAM. ISSN: 0035-3787.
DOCUMENT TYPE: Article
LANGUAGE: French
ENTRY DATE: Entered STN: 24 Apr 2002
Last Updated on STN: 24 Apr 2002

AB During the past 10 years, there has been an increasing interest in the study of rapid-eye-movement (REM) sleep in neurodegenerative diseases and more particularly in Parkinson's disease (PD). This interest is justified by the strong association observed between these diseases and REM sleep behavior disorder (RBD). In the first section of this paper, a critical review of the literature on the presence of REM sleep disorders in PD is presented. Studies that show an association between PD and RBD are reviewed. Studies that report the presence of other REM sleep disorders in PD (short latency, abnormal length and/or proportion of REM sleep, increasing occurrence of hallucinations) are then discussed. Limitations of the criteria proposed by Rechtschaffen et Kales (1968) for the quantification of REM sleep are also presented. Some authors believe that dopaminergic (DA) agents used in the treatment of PD (levodopa, bromocriptine, pergolide, pramipexole and selegiline) could be a responsible factor for the occurrence of REM sleep disorders observed in this disease. The literature concerning the impact of these DA agents on human REM sleep is therefore critically reviewed. It is concluded that DA agents cannot explain on their own the presence of REM sleep disorders in PD. Other causes, among which the disturbance of some neurochemical systems linked to the neuropathological process of the disease, must be considered in order to explain these REM sleep disorders. In the second section of this paper, we present the different pathophysiological hypotheses proposed to explain REM sleep disorders in PD, such as a dysfunction of the cholinergic, noradrenergic, serotonergic, dopaminergic or GABAergic neurons. Emphasis is placed on the role of cholinergic neurons of the pedunculopontine and laterodorsal tegmental nuclei, structures shown to be particularly impaired in PD. Neurophysiological, neuroanatomical and neuropharmacological studies demonstrate that these neurons are strongly implicated in the different REM sleep parameters (muscular atonia, electroencephalographic desynchronisation, ponto-geniculo-occipital spikes). Finally, future research directions are proposed.

L17 ANSWER 2 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:261686 BIOSIS
DOCUMENT NUMBER: PREV200100261686
TITLE: Iron chelating, antioxidant and cytoprotective properties
of dopamine receptor agonist; apomorphine.
AUTHOR(S): Youdim, M. B. H. [Reprint author]; Gassen, M.; Gross, A.;
Mandel, S.; Grunblatt, E.
CORPORATE SOURCE: Department of Pharmacology, Faculty of Medicine, Eve Topf
and National Parkinson's Foundation Centers, Technion,
Haifa, Israel
youdim@tx.technion.ac.il
SOURCE: Journal of Neural Transmission Supplement, (2000)

Vol. 58, pp. 83-96. print.
CODEN: JNTSD4. ISSN: 0303-6995.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 30 May 2001
Last Updated on STN: 19 Feb 2002

AB There have been many attempts to discover neuroprotective drugs for the treatment of Parkinson's disease (PD). Many of these compounds either do not cross the blood brain barrier or are not very effective in the 6-hydroxydopamine or MPTP (N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) models of PD. We have examined several compounds including dopamine receptor agonist bromocriptine, lisuride, pergolide and R-apomorphine for their neuroprotective action against the above neurotoxins in PC12 and dopamine neuroblastoma cell lines in culture and in vivo. R-apomorphine exhibited relatively potent neuroprotective action in vitro, cell culture and in vivo as a radical scavenger and iron chelator, because of its catechol structure. The recent clinical trials with apomorphine, where parkinsonian subjects can be weaned off L-dopa would suggest that this drug either exerts a neuroprotective action or that continuous sustained stimulation of dopamine receptor may be responsible for its unusual pharmacological activity. Apomorphine has a far more broad neuroprotective activity in the various models as compared with l-selegiline and may therefore be an ideal drug to study neuroprotection in parkinsonian subjects with the use of PET or SPECT.

L17 ANSWER 3 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:542644 BIOSIS
DOCUMENT NUMBER: PREV200000542644
TITLE: Pre-clinical studies of pramipexole: Clinical relevance.
AUTHOR(S): Hubble, J. P. [Reprint author]
CORPORATE SOURCE: Department of Neurology, The Ohio State University
Parkinson's Disease Center, 1581 Dodd Drive, Suite 371,
Columbus, OH, 43210, USA
SOURCE: European Journal of Neurology, (May, 2000) Vol.
7, No. Supplement 1, pp. 15-20. print.
ISSN: 1351-5101.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 2000
Last Updated on STN: 11 Jan 2002

AB This paper reviews the preclinical study of the novel dopamine agonist pramipexole and its use in early Parkinson's disease (PD). Emphasis will be given to those properties distinguishing this drug from other dopamine agonists, the relevance of the preclinical data to clinical trial results in early PD, and the putative neuroprotective properties of the compound. The conventional dopamine agonists are ergot-derived compounds that are most widely used as adjunctive therapies in advancing Parkinson's disease (PD). Examples of conventional agonists are bromocriptine and pergolide. Pramipexole is an aminobenzothiazole compound, recently introduced for the treatment of both early and advanced PD. Its nonergot structure may reduce the risk of side-effects, considered unique to ergot drugs, such as membranous fibrosis. Pramipexole is a full dopamine agonist with high selectivity for the D2 dopamine receptor family. This family includes the D2, D3 and D4 receptor subtypes. Pramipexole has a 5- to 7-fold greater affinity for the D3 receptor subtype with lower affinities for the D2 and D4 receptor subtypes. The drug has only minimal alpha2-adrenoceptor activity and virtually no other receptor agonism or antagonism. The optimal dopamine receptor activation for the safe and effective treatment of PD is not known. Findings in animal models and clinical studies indicate that activation of the postsynaptic D2 receptor subtype provides the most

robust symptomatic improvement in PD. Given its pharmacological profile, it is not surprising that pramipexole was found to be effective in ameliorating parkinsonian signs in animal models. This therapeutic effect has been confirmed in clinical trials in both early and advanced PD. In early disease, it provides a clear reduction in the chief motor manifestations of PD and improved activities of daily living. Perhaps most striking is the large number of clinical trial patients who have remained on pramipexole monotherapy for many months. The majority of these subjects have been maintained on pramipexole for an excess of 24 months without requiring additional symptomatic treatment with levodopa. This is in contrast to the general clinical experience with older conventional agonists. Pramipexole also has a favourable pharmacokinetic profile. It is rapidly absorbed with peak levels appearing in the bloodstream within 2 h of oral dosing. It has a high absolute bioavailability of > 90% and can be administered without regard to meals. It has no significant effects on other antiparkinson drugs such as levodopa or selegiline. Its excretion is primarily renal and, thus, has little or no impact on hepatic cytochrome P450 enzymes or other related metabolic pathways. Pramipexole has also been theorized to have 'neuroprotectant' properties. Oxyradical generation is posited as a cause or accelerant of brain nigral cell death in PD. Pramipexole stimulates brain dopamine autoreceptors and reduces dopamine synthesis and turnover which may minimize oxidative stress due to dopamine metabolism. Furthermore, the compound has a low oxidation potential that may serve as an oxyradical scavenger in the PD brain. In summary, pramipexole is a new antiparkinson medication found to have unique dopamine agonist characteristics and putative neuroprotective properties.

L17 ANSWER 4 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
 ACCESSION NUMBER: 1996:475219 BIOSIS
 DOCUMENT NUMBER: PREV199699204775
 TITLE: Drug therapy for Parkinson's disease.
 AUTHOR(S): Charles, P. David [Reprint author]; Davis, Thomas L.
 CORPORATE SOURCE: 352 MCS, 2100 Pierce Ave., Nashville, TN 37212, USA
 SOURCE: Southern Medical Journal, (1996) Vol. 89, No. 9,
 pp. 851-856.
 CODEN: SMJOAV. ISSN: 0038-4348.
 DOCUMENT TYPE: Article
 LANGUAGE: English
 ENTRY DATE: Entered STN: 24 Oct 1996
 Last Updated on STN: 24 Oct 1996

AB Parkinson's disease (PD) is a common neurodegenerative disease characterized by tremor, rigidity, bradykinesia, and loss of postural reflexes. Although the agents available for symptomatic treatment now allow most parkinsonian patients to live a normal life-span, these patients become progressively unable to participate in social functions, perform activities of daily living, and work. Therapy for PD may be associated with many complications that contribute to these disabilities. For this reason, education is helpful for the patient newly diagnosed with PD. Over the past 6 years, three new medications (selegiline, pergolide, and controlled-release levodopa) have been approved for use in Parkinson's disease. Other agents now available for the treatment of psychiatric illness may also be helpful in selected cases of PD. With this in mind, we review the commonly prescribed drugs and outline a rational plan for treatment of parkinsonism.

L17 ANSWER 5 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
 ACCESSION NUMBER: 1996:385106 BIOSIS
 DOCUMENT NUMBER: PREV199699107462
 TITLE: Treatment of early Parkinson's diseases: Are complicated strategies justified?.

AUTHOR(S): Ahlskog, J. Eric
CORPORATE SOURCE: Dep. Neurology, Mayo Clinic Rochester, 200 First St. SW,
Rochester, MN 55905, USA
SOURCE: Mayo Clinic Proceedings, (1996) Vol. 71, No. 7,
pp. 659-670.
CODEN: MACPAJ. ISSN: 0025-6196.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Aug 1996
Last Updated on STN: 26 Aug 1996

AB A variety of medical treatment strategies have been proposed as a means of slowing the progression of Parkinson's disease. This includes administration of selegiline (deprenyl) therapy, early use of bromocriptine or pergolide, and delay of levodopa therapy or restriction of the dose. There is no compelling evidence supporting the use of any of these treatment strategies for this purpose. Carbidopa-levodopa remains the most potent medication for symptomatic treatment of Parkinson's disease. Although starting levodopa therapy with the controlled-release formulation is advocated, this does not appear to have any major advantages over standard carbidopa-levodopa. Further studies are needed to identify other means of halting the progression of Parkinson's disease.

L17 ANSWER 6 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:273901 BIOSIS
DOCUMENT NUMBER: PREV199698830030
TITLE: Current trends in the pharmacologic and surgical treatment of Parkinson's disease.
AUTHOR(S): Galler, Robert Michael [Reprint author]; Hallas, Brian H.; Fazzini, Enrico
CORPORATE SOURCE: 89A Lexington Ave., Second Floor, Westbury, NY 11590, USA
SOURCE: Journal of the American Osteopathic Association, (1996) Vol. 96, No. 4, pp. 228-232.
CODEN: JAOAAZ. ISSN: 0098-6151.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Jun 1996
Last Updated on STN: 10 Jun 1996

AB Recently, there has been a surge in the research regarding the pharmacologic and surgical treatment of Parkinson's disease. This article reviews the latest modes of medical and surgical therapy for Parkinson's disease. The latest drug therapy has consisted of levodopa, a combination of levodopa and carbidopa (Sinemet/Sinemet CR), and monoamine oxidase type B (MAO-B) inhibitors (selegiline hydrochloride). The surgical treatment modalities have been stereotaxic implantations of dopamine-producing tissues (such as adrenal medulla and fetal mesencephalon) into the caudate nucleus and ventral pallidotomy of patients with Parkinson's disease. The most recent work has been in the field of gene therapy. The implantation of cells genetically modified to express trophic factors and tyrosine hydroxylase for the synthesis of L-dopa from tyrosine has been proposed as a possible route for the treatment of Parkinson's disease. Although the etiology of the disease is still unknown, two recent theories are discussed.

L17 ANSWER 7 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:415059 BIOSIS
DOCUMENT NUMBER: PREV199598429359
TITLE: The Therapeutic Potential of Moclobemide, a Reversible Selective Monoamine Oxidase A Inhibitor in Parkinson's disease.
AUTHOR(S): Sieradzan, Katarzyna [Reprint author]; Channon, Shelley; Ramponi, Cristina; Stern, Gerald M.; Lees, Andrew J.;

Youdim, Moussa B. H.
CORPORATE SOURCE: Dep. Neurol., Manchester Royal Infirmary, Oxford Road,
Manchester, M13, UK
SOURCE: Journal of Clinical Psychopharmacology, (1995)
Vol. 15, No. 4 SUPPL. 2, pp. 51S-59S.
CODEN: JCPYDR. ISSN: 0271-0749.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Sep 1995
Last Updated on STN: 27 Sep 1995

AB Dopamine is equally well deaminated oxidatively by monoamine oxidase (MAO) A and B types. Selegiline (L-deprenyl), a selective inhibitor of MAO-B, ameliorates the "wearing off" akinesia and delays the need for levodopa in mild, previously untreated Parkinson's disease. The therapeutic potential of selective inhibition of MAO-A in Parkinson's disease has not been examined in detail. MAO-A accounts for only about 20% of total MAO activity in the human basal ganglia, and it differs from MAO-B in distribution. In contrast to MAO-B, which is confined to the extraneuronal compartment, MAO-A is found both extraneuronally and within the presynaptic dopaminergic terminals. The inhibition of MAO-A might alter the intraneuronal handling of dopamine reuptaken from synaptic clefts and thereby prolong oral levodopa benefit. We have given moclobemide, a selective, reversible inhibitor of MAO-A, to nondepressed patients with Parkinson's disease receiving standard levodopa/peripheral decarboxylase inhibitor or levodopa with dopaminergic agonist (bromocriptine, pergolide). Selegiline was discontinued at least 8 weeks earlier. A standard oral levodopa challenge was performed at the patient's entry to the study and repeated on the 22nd day of moclobemide treatment (150 mg thrice daily). The overall time spent "on" and "off" before the onset of treatment and during the last week on the drug was estimated from the patients' diaries. Neuropsychological assessments were also made before and after 3 weeks of moclobemide to measure possible effects on cognitive performance and mood. In acute levodopa challenge, the latency of motor response was significantly shortened and its duration was prolonged during moclobemide treatment. Similarly, the Webster's scores in "off" state after overnight withdrawal of dopaminergic medication improved on moclobemide. In nondepressed parkinsonian patients, moclobemide did not alter mood and cognitive measures. The mild symptomatic effect and good tolerance with standard therapy suggest that moclobemide may be a particularly useful antidepressant in Parkinson's disease.

L17 ANSWER 8 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:83090 BIOSIS
DOCUMENT NUMBER: PREV199598097390
TITLE: Early idiopathic parkinsonism: Initiation and optimization
of treatment.
AUTHOR(S): Calne, Donald B.
CORPORATE SOURCE: Neurodegenerative Disorders Cent., Faculty Med., Vancouver
Hosp., Purdy Pavillion, 2211 Wesbrook Mall, Vancouver, BC
V6T 2B5, Canada
SOURCE: Clinical Neuropharmacology, (1994) Vol. 17, No.
SUPPL. 2, pp. S14-S18.
CODEN: CLNEDB. ISSN: 0362-5664.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Feb 1995
Last Updated on STN: 23 Feb 1995

AB Once a diagnosis of idiopathic parkinsonism has been made, the choice and timing of therapy depend almost entirely on the patient's need for symptomatic relief, as no presently available therapy has any effect on the pathogenesis of the disease. Five categories of drugs are

available for the treatment of idiopathic parkinsonism. Anticholinergic agents are effective against tremor but have prominent adverse effects. Amantadine has similar effects but is more active against rigidity and bradykinesia. Selegiline is a monoamine oxidase-B inhibitor: once thought to affect the pathogenesis of idiopathic parkinsonism, it is now known to offer only symptomatic relief. The dopamine agonists (bromocriptine, pergolide, and lisuride) stimulate D-2 receptors: they have antiparkinsonian effects and tolerance profiles broadly similar to those of levodopa but are slightly less efficacious. Pleural effusions and pulmonary fibrosis are unusual but important complication, of these drugs: chest x-ray examinations are therefore recommended for all patients starting such treatment. Levodopa (combined with an extracerebral decarboxylase inhibitor to prevent nausea, the main adverse effect) has become the standard antiparkinsonism treatment. Patients using this preparation can suffer considerable variations in mobility and dyskinesia, which may be related to rapid, large-scale oscillations in plasma levodopa concentrations. Controlled-release (CR) preparations have been developed in an attempt to minimize these fluctuations and reduce long-term side effects. There is no universally agreed treatment for idiopathic parkinsonism. However, experience shows that a good balance of antiparkinsonian activity and adverse effects can be obtained by initiating treatment with a combination of levodopa and a decarboxylase inhibitor. A dopamine agonist can be added if the disease progresses and increased therapeutic activity is required.

L17 ANSWER 9 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
 ACCESSION NUMBER: 1994:165810 BIOSIS
 DOCUMENT NUMBER: PREV199497178810
 TITLE: An analysis of treatment options and outcome in patients with Parkinson's disease and severe dyskinesias.
 AUTHOR(S): Mark, Margery H.,; Sage, Jacob I. [Reprint author]
 CORPORATE SOURCE: Dep. Neurol., UMDNJ-Robert Wood Johnson Med. Sch., CN-19, New Brunswick, NJ 08903, USA
 SOURCE: Annals of Clinical and Laboratory Science, (1994) Vol. 24, No. 1, pp. 12-21.
 CODEN: ACLSCP. ISSN: 0091-7370.
 DOCUMENT TYPE: Article
 LANGUAGE: English
 ENTRY DATE: Entered STN: 8 Apr 1994
 Last Updated on STN: 10 Apr 1994

AB Forty-one patients with Parkinson's disease and severe dyskinesias were analyzed retrospectively to determine if some general principles would emerge to aid physicians handling this complication of treatment. Dyskinesia type (high dopa chorea (HDC), low dopa chorea (LDC), high dopa dystonia (HDD), and low dopa dystonia (LDD)) predicted response to treatment and whether or not levodopa dose reduction would benefit dyskinesias without producing unacceptable "offs." High dopa chorea improved best but at the expense of increased "off" time, followed by LDD, HDD, and LDC. Levodopa reduction was an acceptable strategy in ameliorating HDC and LDD only. Adjunctive therapy benefitted all dyskinesia types, although the majority of patients (12/17) helped by selegiline had LDD or LDC. Generally, low doses of dopamine agonists were helpful (bromocriptine lt 20 mg/day; pergolide lt 2 mg/day). When adding adjunctive therapy (except for selegiline or controlled-release carbidopa/levodopa), concomitant reduction in daily dose of levodopa was not an effective strategy to decrease dyskinesias. Serial trials of multiple drug regimens are useful in these patients.

L17 ANSWER 10 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
 ACCESSION NUMBER: 1992:283211 BIOSIS

DOCUMENT NUMBER: PREV199294007861; BA94:7861
TITLE: PARKINSONISM TREATMENT PART III. UPDATE.
AUTHOR(S): COLLIER D S [Reprint author]; BERG M J; FINCHAM R W
CORPORATE SOURCE: COLLEGE PHARMACY, UNIVERSITY IOWA, IOWA CITY, IOWA 52242, USA
SOURCE: Annals of Pharmacotherapy, (1992) Vol. 26, No. 2, pp. 227-233.
CODEN: APHRER. ISSN: 1060-0280.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 10 Jun 1992
Last Updated on STN: 10 Jun 1992

AB Objective: The purpose of this review is to update clinicians with recent advances in the management of parkinsonism, including drug therapy, transplantation, and diet. Data sources: Pertinent articles were obtained from an English-language literature search using MEDLINE (1970-1991), Index Medicus (1987-1991), Current Contents (1990), and bibliographic reviews of review articles. Index terms included parkinsonism, selegiline, pergolide, vitamin E, and transplantation. Fifty-five articles (representing 85 percent of the complete literature search) were selected by multiple reviewers for their contribution to the stated purpose. Emphasis was placed on double-blind, placebo-controlled, and randomized studies. Data from cited articles were examined by multiple reviewers for support of their stated hypothesis and were included as background for justification of major points in this article; critical studies were abstracted in more detail. Results: New therapeutic measures have been added to the treatment of parkinsonism. Selegiline, a monoamine oxidase inhibitor type B, has shown beneficial results, especially in early stages. Pergolide, a dopamine agonist, may be an efficacious alternative to bromocriptine resistance or intolerable adverse effects. Vitamin E may have protective antioxidant properties, but very few clinical data are available. Fetal tissue transplantation needs continued research and remains very controversial. Diet modifications may maximize the results of therapy with exogenous dopamine therapy. Conclusions: Clinicians should familiarize themselves with new alternatives for the management of parkinsonism in order to be reliable consultants for both professional and lay persons.

L17 ANSWER 11 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 1991:140709 BIOSIS
DOCUMENT NUMBER: PREV199191077249; BA91:77249
TITLE: EARLY COMBINATION OF SELEGILINE AND LOW-DOSE L DOPA AS INITIAL SYMPTOMATIC THERAPY IN PARKINSON'S DISEASE EXPERIENCE IN 26 PATIENTS RECEIVING COMBINED THERAPY FOR 26 MONTHS.
AUTHOR(S): ELIZAN T S [Reprint author]; MOROS D A; YAHR M D
CORPORATE SOURCE: DEP NEUROLOGY, BOX 1137, MOUNT SINAI MED CENTER, 1 GUSTAVE L LEVY PL, NEW YORK NY 10029, USA
SOURCE: Archives of Neurology, (1991) Vol. 48, No. 1, pp. 31-34.
CODEN: ARNEAS. ISSN: 0003-9942.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 14 Mar 1991
Last Updated on STN: 22 May 1991

AB Thirty-eight patients newly diagnosed as having Parkinson's disease (mean age, 57.3 years; mean Parkinson's disease duration, 2.7 years) in the earlier phase of the disease (mean Hoehn/Yahr

stage, 2; mean motor scores, 11.4) were given selegiline (Deprenyl), 10 mg daily, and maintained on this drug alone until significant clinical worsening warranted the addition of low-dose levodopa (Sinemet, 25/100 three to four doses per day). Five of these patients were not yet receiving additional levodopa despite some worsening of motor scores. Of the 33 patients now taking combined therapy, seven have been followed up for 6 months or less. Twenty-four (92%) of the 26 patients taking combined therapy for a mean of 26 months (8.5 to 99 months) who have had Parkinson's disease for 6 years showed a dramatic improvement in their parkinsonism shortly after the addition of levodopa, with significant decreases in their rated motor scores, such improvement being maintained at their latest neurologic evaluation. Eighteen (75%) of these 24 patients responded to the combined selegiline/levodopa therapy with degrees of improvement equal to or greater than 50%, compared with their motor status at the start of combined therapy just before the addition of levodopa. This degree of "reversal" of parkinsonism on addition of levodopa (mean carbidopa/levodopa dose, 98/380 mg) was not observed in any of these same patients receiving selegiline alone for an average of 13.8 months. Four patients taking combined therapy developed mild, transient, abnormal involuntary movements, and end-of-dose pattern of response after more than 2 years of combined therapy (24.75 and 33.5 months, respectively). Our results on combined selegiline/levodopa therapy reemphasize the continuing dominant role of levodopa as the primary drug for the symptomatic treatment of Parkinson's disease. A possible synergistic role of selegiline with levodopa in the early cases is suggested by the sustained therapeutic effectiveness of even low doses of the latter for a period of 26 months, with a delay in the appearance of relatively minor side effects developing only after more than 2 years of combined therapy. At an average disease duration of 6 years, no patient has had a major functional disability. A concurrently studied control group of patients treated with low-dose levodopa alone, or one treated with a combination of low-dose levodopa and a dopamine agonist like bromocriptine or pergolide, may have clarified further the role of selegiline, but such control subjects were not available to us at this time. We suggest the early combination of a selective monoamine oxidase type B inhibitor like selegiline, and the original dopamine replacement drug, levodopa (as low-dose Sinemet), as initial symptomatic therapy in newly diagnosed cases of Parkinson's disease.

L17 ANSWER 12 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:929529 CAPLUS

DOCUMENT NUMBER: 139:127105

TITLE: Dopamine agonist monotherapy in Parkinson's disease

AUTHOR(S): Clarke, C. E.; Guttman, M.

CORPORATE SOURCE: Department of Neurology, City Hospital, University of Birmingham, Birmingham, B18 7QH, UK

SOURCE: Lancet (2002), 360(9347), 1767-1769

CODEN: LANCAO; ISSN: 0140-6736

PUBLISHER: Lancet Publishing Group

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Levodopa is the gold-standard therapy for Parkinson's disease. However, long-term treatment leads to involuntary movements and response fluctuations which add to the complexities of later disease-management. In addition, preclin. evidence suggests that levodopa is toxic to dopaminergic neurons. These problems have led to a move away from levodopa toward initial monotherapy with a dopamine agonist. Positron-emission tomog. (PET) and single-photon emission computed tomog. (SPECT) tracers have been developed which may be considered surrogate markers for remaining dopaminergic neurons. In a randomized controlled

trial in patients with early Parkinson's disease, the Parkinson Study Group used 123I-β-CIT SPECT. Those patients given pramipexole had significantly reduced loss of striatal uptake at 46 mo compared with those given levodopa (16.0% vs. 25.5%). A similar trial used 18F-DOPA PET. Patients given ropinirole had significantly reduced loss of striatal uptake at 24 mo compared with those given levodopa (13% vs. 20%). These studies suggest that agonist monotherapy may be neuroprotective and/or that levodopa is toxic. This work has been criticized, as the SPECT results may have resulted from a differential effect of the agonist and levodopa on the regulation of the dopamine transporter, thereby influencing the imaging outcome measure. Other criticisms include insufficient data on the use of the potential neuroprotectant selegiline and patients on pramipexole in the SPECT study appear to have been clin. slow progressors. Single clin. trials with each of the four modern agonists compared with levodopa show that as monotherapy the agonists delay the onset of involuntary movements, although at the expense of poorer treatment of motor impairments and disability and more dopaminergic adverse events. The only health-related quality of life data show no difference between pramipexole and levodopa after 4 yr. No information on health-economics measures is available but agonists cost two to three times as much as levodopa. Young patients should be treated with agonist monotherapy since the trials included predominantly younger patients who have a higher incidence of motor complications. Those with significant co-morbidity, dementia, or a short life-expectancy should be treated with the lowest dose of levodopa required to maintain motor function. For the vast majority though, no clear guidance can be given. Further large-scale pragmatic trials in large nos. of patients over prolonged periods are urgently required.

OS.CITING REF COUNT: 31 THERE ARE 31 CAPLUS RECORDS THAT CITE THIS RECORD (31 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 13 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:450602 CAPLUS

DOCUMENT NUMBER: 137:56883

TITLE: Clinical pharmacokinetic and pharmacodynamic properties of drugs used in the treatment of Parkinson's disease

AUTHOR(S): Deleu, Dirk; Northway, Margaret G.; Hanssens, Yolande
CORPORATE SOURCE: College of Medicine, Sultan Qaboos University, Al Khod, Oman

SOURCE: Clinical Pharmacokinetics (2002), 41(4), 261-309

CODEN: CPKNDH; ISSN: 0312-5963

PUBLISHER: Adis International Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Current research in Parkinson's disease (PD) focuses on symptomatic therapy and neuroprotective interventions. Drugs that have been used for symptomatic therapy are levodopa, usually combined with a peripheral decarboxylase inhibitor, synthetic dopamine receptor agonists, centrally-acting antimuscarinic drugs, amantadine, monoamine oxidase-B (MAO-B) inhibitors and catechol-O-methyltransferase (COMT) inhibitors. Drugs for which there is at least some evidence for neuroprotective effect are certain dopamine agonists, amantadine and MAO-B inhibitors (selegiline). Levodopa remains the most effective drug for the treatment of PD. Several factors contribute to the complex clin. pharmacokinetics of levodopa: erratic absorption, short half-life, peripheral O-methylation and facilitated transport across the blood-brain barrier. In patients with response fluctuations to levodopa, the concentration-effect curve becomes steeper and shifts to the right compared with

patients with stable response. Pharmacokinetic-pharmacodynamic modeling can affect decisions regarding therapeutic strategies. The dopamine agonists include ergot derivs. (bromocriptine, pergolide, lisuride and cabergoline), non-ergoline derivs. (pramipexole, ropinirole and piribedil) and apomorphine. Most dopamine agonists have their specific pharmacol. profile. They are used in monotherapy and as an adjunct to levodopa in early and advanced PD. Few pharmacokinetic and pharmacodynamic data are available regarding centrally acting antimuscarinic drugs. They are characterized by rapid absorption after oral intake, large volume of distribution and low clearance relative to hepatic blood flow, with extensive metabolism. The mechanism of action of amantadine remains elusive. It is well absorbed and widely distributed. Since elimination is primarily by renal clearance, accumulation of the drug can occur in patients with renal dysfunction and dosage reduction must be envisaged. The COMT inhibitors entacapone and tolcapone dose-dependently inhibit the formation of the major metabolite of levodopa, 3-O-methyldopa, and improve the bioavailability and reduce the clearance of levodopa without significantly affecting its absorption. They are useful adjuncts to levodopa in patients with end-of-dose fluctuations. The MAO-B inhibitor selegiline may have a dual effect: reducing the catabolism of dopamine and limiting the formation of neurotoxic free radicals. The pharmacokinetics of selegiline are highly variable; it has low bioavailability and large volume of distribution. The oral clearance is many-fold higher than the hepatic blood flow and the drug is extensively metabolized into several metabolites, some of them being active. Despite the introduction of several new drugs to the antiparkinsonian armamentarium, no single best treatment exists for an individual patient with PD. Particularly in the advanced stage of the disease, treatment should be individually tailored.

OS.CITING REF COUNT: 66 THERE ARE 66 CAPLUS RECORDS THAT CITE THIS
RECORD (66 CITINGS)
REFERENCE COUNT: 303 THERE ARE 303 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L17 ANSWER 14 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:49017 CAPLUS

DOCUMENT NUMBER: 135:86375

TITLE: Iron chelating, antioxidant and cytoprotective
properties of dopamine receptor agonist; apomorphine
AUTHOR(S): Youdim, M. B. H.; Gassen, M.; Gross, A.; Mandel, S.;
Grunblatt, E.

CORPORATE SOURCE: Department of Pharmacology, Eve Topf and National
Parkinson's Foundation Centers, Bruce Rappaport Family
Research Institute, Faculty of Medicine, Haifa, Israel
SOURCE: Advances in Research on Neurodegeneration (

2000), 7(7th International Winter Conference

on Neurodegeneration, 1999), 83-96

CODEN: ARNEFX; ISSN: 1068-719X

PUBLISHER: Springer-Verlag Wien

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 30 refs. There have been many attempts to discover
neuroprotective drugs for the treatment of Parkinson's disease
(PD). Many of these compds. either do not cross the blood brain barrier
or are not very effective in the 6-hydroxydopamine or MPTP
(N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) models of PD. We have
examined several compds. including dopamine receptor agonist bromocriptine,
lisuride, pergolide and R-apomorphine for their neuroprotective
action against the above neurotoxins in PC12 and dopamine neuroblastoma
cell lines in culture and in vivo. R-apomorphine exhibited relatively
potent neuroprotective action in vitro, cell culture and in vivo as a

radical scavenger and iron chelator, because of its catechol structure. The recent clin. trials with apomorphine, where parkinsonian subjects can be weaned off L-dopa would suggest that this drug either exerts a neuroprotective action or that continuous sustained stimulation of dopamine receptor may be responsible for its unusual pharmacol. activity. Apomorphine has a far more broad neuroprotective activity in the various models as compared with l-selegiline and may therefore be an ideal drug to study neuroprotection in parkinsonian subjects with the use of PET or SPECT.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD
(3 CITINGS)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 15 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:92856 CAPLUS

DOCUMENT NUMBER: 132:117010

TITLE: Comparative tolerability of the newer generation
antiparkinsonian agents

AUTHOR(S): Lambert, Dorothee; Waters, Cheryl H.

CORPORATE SOURCE: Department of Neurology, Division of Movement
Disorders, University of Southern California, Los
Angeles, CA, USA

SOURCE: Drugs & Aging (2000), 16(1), 55-65

CODEN: DRAGE6; ISSN: 1170-229X

PUBLISHER: Adis International Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 44 refs. In recent years, the treatment of Parkinson's disease has undergone an immense amount of research, resulting in the development of multiple new medications. This has largely been fuelled by dissatisfaction over the development of motor complications secondary to long term levodopa therapy. Different treatment approaches are applied depending on the stage of Parkinson's disease. In early and mild Parkinson's disease, selegiline offers a limited symptomatic effect. Its neuroprotective effect, although at present theor., has questionable clin. relevance. Increased mortality associated with selegiline has been reported, although a meta-anal. of 5 different trials did not support this finding. The newer, non-ergoline dopamine agonists, pramipexole and ropinirole, have undergone extensive studies to evaluate their efficacy as monotherapy in early Parkinson's disease. These newer agonists are ideal initial symptomatic medications, primarily because they delay the onset of levodopa-induced motor fluctuations. Efficacy of the newer dopamine agonists in advanced disease seems to be comparable to that of the older agents, bromocriptine and pergolide. Adverse effects can be reduced by starting the medication at a very low dose and then slowly titrating upward. Catechol-O-Me transferase (COMT) inhibitors are indicated for the treatment of motor fluctuations in advanced disease, particularly the "wearing-off" phenomenon. Tolcapone, a peripheral and central COMT inhibitor, appears to be quite effective, producing a 47% reduction in "off" time. Unfortunately, 3 deaths have been observed, which are presumably secondary to tolcapone therapy. The drug has been withdrawn in many countries, and liver enzyme testing is mandatory in the US. Entacapone, a purely peripheral COMT inhibitor with a lower potency than tolcapone, has also proved to be effective and has not been associated with liver damage, obviating the need for testing.

OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS
RECORD (10 CITINGS)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 16 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1999:150305 CAPLUS
DOCUMENT NUMBER: 130:261327
TITLE: Ropinirole: a dopamine agonist for the treatment of Parkinson's disease
AUTHOR(S): Kuzel, Mary D.
CORPORATE SOURCE: Pharmacy Practice, College of Pharmacy, North Dakota State University, Fargo, ND, 58103, USA
SOURCE: American Journal of Health-System Pharmacy (1999), 56(3), 217-224
CODEN: AHSPEK; ISSN: 1079-2082
PUBLISHER: American Society of Health-System Pharmacists
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 42 refs. The pharmacol., pharmacokinetics, clin. efficacy, adverse effects, dosage and administration, and formulary considerations of ropinirole are reviewed. Ropinirole is a nonergoline dopamine agonist that binds to dopamine D2-receptors; the drug is indicated for use in the symptomatic treatment of early and late Parkinson's disease (PD). Ropinirole is rapidly absorbed after oral administration and undergoes extensive hepatic metabolism to active metabolites. The elimination half-life av. about six hours. Ropinirole has a low potential to interact with other drugs likely to be administered to PD patients. In patients with early PD, initial monotherapy with ropinirole was more effective than placebo or bromocriptine in the absence of selegiline and was as effective as bromocriptine in the presence of selegiline. Ropinirole was as effective as levodopa in patients with earlier stages of PD. In one subset of patients with advanced PD not adequately controlled by levodopa, adjunctive ropinirole was more effective than placebo and bromocriptine. Ropinirole was more effective than bromocriptine in patients previously given high-dose levodopa and was as effective in patients previously given low-dose levodopa or adjunctive dopamine agonist therapy. The most frequent adverse effects are nausea, somnolence, and dizziness; the dosage should be increased gradually to minimize adverse effects. Ropinirole is less expensive than bromocriptine and pergolide and similar in cost to pramipexole. Ropinirole appears to be a useful addition to existing therapeutic approaches to PD and is approved for both early and later stages of the disease.

OS.CITING REF COUNT: 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 17 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1997:422228 CAPLUS
DOCUMENT NUMBER: 127:103729
ORIGINAL REFERENCE NO.: 127:19807a,19810a
TITLE: Pharmacologic options for managing Parkinson's disease
AUTHOR(S): Evidente, Virgilio G. H.; Adler, Charles H.
CORPORATE SOURCE: Mayo Clinic, Scottsdale, AZ, USA
SOURCE: Formulary (1997), 32(6), 594-596, 601-602, 604, 607-610
CODEN: FORMF9; ISSN: 1082-801X
PUBLISHER: Advanstar
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 54 refs. Current therapy for idiopathic Parkinson's disease (IPD) is mainly symptomatic with the focus on individualizing therapy for early and advanced stage disease. The most effective drug for both early and advanced IPD is levodopa. For patients with mild disease and minimal disability, monotherapy with anticholinergic agents,

amantadine, selegiline, or dipamine agonists (eg, bromocriptine and pergolide) may be useful. Advanced disease is usually associated with levodopa-induced complications, such as motor fluctuations and dyskinesias, which may be alleviated by adjusting levodopa dosing or by adding a dopamine agonist. Although no drug has been unequivocally proven to be neuroprotective in IPD, selegiline, amantadine, bromocriptine, and pergolide may play some role in delaying the progression of disease.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 18 OF 76 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003014025 EMBASE
TITLE: Beyond the iron mask: Towards better recognition and treatment of depression associated with Parkinson's disease.
AUTHOR: Burn, David J., Dr. (correspondence)
CORPORATE SOURCE: Regional Neurosciences Centre, Newcastle General Hospital, University of Newcastle upon Tyne, Newcastle upon Tyne, United Kingdom. d.j.burn@ncl.ac.uk
AUTHOR: Burn, David J., Dr. (correspondence)
CORPORATE SOURCE: Regional Neurosciences Centre, Newcastle Hospital, Westgate Road, Newcastle upon Tyne NE4 6BE, United Kingdom. d.j.burn@ncl.ac.uk
SOURCE: Movement Disorders, (May 2002) Vol. 17, No. 3, pp. 445-454.
Refs: 103
ISSN: 0885-3185 CODEN: MOVDEA
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Jan 2003
Last Updated on STN: 29 Jan 2003

AB This review examines the frequency of depression complicating Parkinson's disease (PD), its aetiology and clinical features, and also how it may be recognised and treated. Studies investigating the frequency of depression in PD have yielded figures ranging between 2.7% and 70%. Methodological differences account for much of the disparity. The aetiology of depression in PD is complex, and probably relates to both biological and exogenous factors. Dysfunction of multiple neurotransmitter systems, including the serotonergic system, may be involved. Mood disturbances resulting from deep brain stimulation of the subthalamic nucleus may provide a fruitful area for future research, and assist our understanding of the neural networks involved in mediating depression. Several recent studies have confirmed that depression in the PD patient is a major determinant of quality of life and that this is closely related to dysfunction in other clinically important health areas. The validity for many existing scales in the screening, diagnosis, and monitoring of depression in the PD patient has not been established. The Montgomery-Asberg Depression Rating Scale and the Hamilton Rating Scale for Depression appear to have good diagnostic sensitivity and specificity when compared with DSM-IV criteria. Recommendations for the optimal drug treatment of depression in PD are difficult to give, due to an

inexplicable dearth of sizeable, placebo-controlled studies. A majority of physicians would probably now opt for a selective serotonin reuptake inhibitor in the depressed PD patient. There is no good evidence that these drugs are associated with a worsening of motor features, but they should probably not be coprescribed with selegiline, because of the risk of causing a potentially serious serotonin syndrome. Several studies have suggested that depression in the PD patient is associated with a more rapid deterioration in cognitive and motor functions, perhaps as a surrogate marker for more extensive brainstem cell loss. .COPYRGT. 2002 Movement Disorder Society.

L17 ANSWER 19 OF 76 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2002355398 EMBASE
TITLE: Practical importance of neuroprotection in Parkinson's disease.
AUTHOR: Riederer, Peter (correspondence); Gille, G.; Muller, T.; Przuntek, H.; Reichmann, H.; Riess, O.; Schwartz, A.; Schwarz, J.; Vogt, T.
CORPORATE SOURCE: Clinical Neurochemistry, Clin./Policlin. Psychiat./Psychothr., University of Wurzburg, 97080 Wurzburg, Germany. peter.riederer@mail.uni-wuerzburg.de
SOURCE: Journal of Neurology, Supplement, (2002) Vol. 249, No. 3, pp. III53-III56.
Refs: 11
ISSN: 0939-1517 CODEN: JNSUE6
COUNTRY: Germany
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Oct 2002
Last Updated on STN: 24 Oct 2002

AB Consensus could be reached that there is overwhelming evidence of preclinical neuroprotection. However, the evidence of neuroprotection/neurorescue under clinical conditions is limited. Lessons from clinical trials designed to show neuroprotection (selegiline, amantadine, dopamine agonists) demonstrate that with the drugs available neuroprotection/neurorescue has to start as early as possible. A PET-controlled clinical trial with ropinirole shows that there seems to be a good chance for neuroprotection in the early phase of Parkinson's disease in patients treated from the very beginning of the disease while there is no such benefit in patients with a late start of a neuroprotective therapeutic strategy. Also long-term clinical neuroprotection cannot be reached. Complicating factors to demonstrate clinical neuroprotection are discussed.

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ACCESSION NUMBER: 2002328044 EMBASE
TITLE: [The evolution of use of anti-Parkinson drugs in Spain]. Evolucion del consumo de farmacos antiparkinsonianos en Espana.
AUTHOR: Montane, E.; Vallano, A., Dr. (correspondence); Castel, J.M.
CORPORATE SOURCE: Servicio de Farmacologia Clinica, Hospital Universitario Vall d'Hebron, Passeig de la Vall d'Hebron, 119-129 E-08035 Barcelona, Spain. tv@icf.uab.es
SOURCE: Revista de Neurologia, (1 Apr 2002) Vol. 34, No. 7, pp. 612-617.

Refs: 43
ISSN: 0210-0010 CODEN: RVNRAA
COUNTRY: Spain
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 036 Health Policy, Economics and Management
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: Spanish; Castilian
SUMMARY LANGUAGE: English; Spanish; Castilian; Portuguese
ENTRY DATE: Entered STN: 3 Oct 2002
Last Updated on STN: 3 Oct 2002

AB Introduction. In recent years new anti-Parkinson drugs have been marketed and there has been controversy over the safety of some drugs. Objective. To analyze the evolution of the consumption of anti-Parkinson drugs and the effect of the newer drugs. Patients and methods. A study of the consumption of anti-Parkinson drugs (1989-1998). Data were obtained from the ECOM database of the Ministry of Health and TEMPUS of the National Statistics Institute. The drugs were classified using the Anatomic-Therapeutic-Clinical Classification (ATC). Consumption was expressed in defined daily dosage (DDD) and the costs in euros (€). The drugs marketed since 1990 were classified as new drugs and the others as classical drugs. Results. The total consumption of drugs increased from 1.92 DDD/1,000 inhabitants/day in 1989 to 3.64 DDD/1,000 inhabitants/day in 1998. The drugs showing the greatest increase were selegiline, pergolide and levodopa. The total pharmaceutical expenses tripled. There was a smaller increase in the consumption of new drugs (1.2% of the total in 1991 and 6.6% in 1998) than in their costs (6.7% of the total in 1991 and 38.8% in 1998). The cost per DDD of the new drugs increased five times (1989: 2.55€ and 1998: 13.59€) and that of the classical drugs was similar (1989: 0.54€ and 1998: 0.62€). Conclusions. The total consumption of anti-Parkinson drugs has progressively increased. The consumption of selegiline has also increased in spite of controversy over its safety. The new drugs have a major economic effect.

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ACCESSION NUMBER: 2002036123 EMBASE
TITLE: [Switch from conventional selegiline to xilopar® allows dose reduction of levodopa and dopamine agonists].
Umstellung von konventionellen selegilin-preparaten auf xilopar® ermöglicht die reduktion von l-dopa und dopamin-agonisten.
AUTHOR: Holtmann, Wolfgang, Dr. (correspondence)
CORPORATE SOURCE: Arzt fur Neurologie, Schlossplatz 6, 91207 Lauf, Germany.
SOURCE: Neurologie und Rehabilitation, (2001) Vol. 7, No. 6, pp. 298-300.

Refs: 4
ISSN: 0947-2177 CODEN: NEREF3
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: German
SUMMARY LANGUAGE: English; German
ENTRY DATE: Entered STN: 7 Feb 2002
Last Updated on STN: 7 Feb 2002

AB The anti-parkinsonian drug selegiline has successfully been used for years in order to achieve a levodopa sparing effect. The need for levodopa therapy can be delayed by an average of 9 months. In addition, various placebo-controlled studies demonstrated that the levodopa dose can be maintained almost stable for a period of at least 5

years when used in combination with selegiline. On the other hand, therapy with conventional selegiline is limited, e. g. by the contra-indication in patients with impaired hepatic or renal function, the possible disturbance of night-time sleep by the amphetamine metabolites, and by the high variability in bioavailability because of an extensive first-pass effect. In Xilopar®, selegiline is presented as a lyophilised tablet that can circumvent these problems. In this case report, the switch from conventional selegiline to Xilopar® lead to a dose reduction of levodopa as well as pergolide associated with very good symptom control. Xilopar® was well tolerated and resulted in a considerable improvement of the patient's quality of life.

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ACCESSION NUMBER: 2001368247 EMBASE
 TITLE: Drug-induced psychotic symptoms in Parkinson's disease. Problems, management and dilemma.
 AUTHOR: Kuzuhara, S., Dr. (correspondence)
 CORPORATE SOURCE: Department of Neurology, Mie University School of Medicine, Tsu, Mie-ken 514-8507, Japan. kuzuhara@clin.medic.mie-u.ac.jp
 SOURCE: Journal of Neurology, Supplement, (2001) Vol. 248, No. 3, pp. 28-31.
 Refs: 16
 ISSN: 0939-1517 CODEN: JNSUE6
 COUNTRY: Germany
 DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
 FILE SEGMENT: 032 Psychiatry
 037 Drug Literature Index
 038 Adverse Reactions Titles
 008 Neurology and Neurosurgery
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 2 Nov 2001
 Last Updated on STN: 2 Nov 2001

AB Psychotic symptoms develop in 20-30% of patients with Parkinson's disease (PD) receiving chronic anti-PD medications, and visual hallucinations with or without delirium and paranoid delusions are the most frequent symptoms. Psychotic symptoms disturb ADL and QOL of PD patients and tax caregivers far more than the motor disabilities do, and good management of drug-induced psychotic symptoms is potentially important. Withdrawal of anti-PD drugs relieves the patients from psychotic side effects, but worsens the parkinsonian motor symptoms. The first step of treatment is to eliminate triggering factors other than anti-PD drugs, such as infections, metabolic disorders, subdural hematoma, and hallucinogenic drugs. The second step is to eliminate anti-PD drugs in the following order; first anticholinergics, amantadine and selegiline, second dopamine agonists, and finally levodopa/carbidopa. Anti-PD medications should be reduced to the point of improving psychotic side effects without drastically worsening parkinsonian motor symptoms. When the above adjustments fail to sufficiently alleviate psychotic side effects, the third step is consideration of antipsychotic drugs although they have potential capacity to antagonize dopamine D2 receptors and worsen parkinsonism. Atypical antipsychotics such as clozapine and olanzapine are recommended, though the former is not available in Japan.

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ACCESSION NUMBER: 2001334888 EMBASE
 TITLE: [Dopaminomimetic psychosis in Parkinson's disease: First

symptom of early dementia?].

Psicosis inducida por farmacos dopaminomimeticos en la enfermedad de Parkinson idiopatica: Primer sintoma de deterioro cognitivo?.

AUTHOR: Catalan-Alonso, Ma.J., Dr. (correspondence); Del Val, J.
CORPORATE SOURCE: Servicio de Neurologia, Unidad de Trastornos del Movimiento, Hospital Clinico San Carlos, Martin Lagos, s/n, E-28040 Madrid, Spain. mcatalan@hcsc.es
SOURCE: Revista de Neurologia, (2001) Vol. 32, No. 11, pp. 1085-1087.
Refs: 7
ISSN: 0210-0010 CODEN: RVNRAA
COUNTRY: Spain
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: Spanish; Castilian
SUMMARY LANGUAGE: English; Spanish; Castilian; Portuguese
ENTRY DATE: Entered STN: 11 Oct 2001
Last Updated on STN: 11 Oct 2001

AB Introduction. Parkinson's disease (PD) is caused by an abnormal degeneration of the dopamine producing cells in the substantia nigra and ventral tegmental area. When PD advances, degeneration of the nigrostriatal tracts may expand and involve other pathways (mesolimbic and frontal), and also serotonergic and cholinergic systems. This degeneration leads to a multitude of motor and non-motor behavioral disturbances. Development. On the background of progressive degeneration, chronic levodopa and dopaminergic agonist administration may cause pulsatile non-physiologic overstimulation of dopaminergic receptors. This may induce perturbations in limbic and frontal cortex structures and overstimulation of serotonergic, cholinergic and other neurotransmitter systems. These events are the basis of parkinsonian psychosis, perhaps in the setting of early dementia. The treatment of this psychosis is difficult. The reduction or withdrawal of dopaminomimetic agents may improve psychosis with worsening of parkinsonian disability. The recommended order to discontinue antiparkinsonian drugs, when is required, is anticholinergic, selegiline, amantadine and dopamine agonist. Levodopa should be reduced to a tolerable minimum to compensate the motor disturbances. At this point, it may be necessary to add an atypical neuroleptic such as clozapine, quetiapine or olanzapine to improve the symptomatology. Conclusions. More studies are needed to assess the relationship between parkinsonian psychosis and early dementia. Additional, the development of new drugs could be helpful to control these psychotic symptoms in PD without serious secondary effects.

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ACCESSION NUMBER: 2001212834 EMBASE
TITLE: [Pharmacotherapy of idiopathic parkinson's syndrome with special focus on neuroprotection].
Pharmakotherapie des idiopathischen parkinson-syndroms unter besonderer berucksichtigung neuroprotektiver therapiestrategien.
AUTHOR: Reichmann, H., Dr. (correspondence); Sommer, U.; Gerlach, M.; Riederer, P.
CORPORATE SOURCE: Klinik und Poliklinik fur Neurologie, Univ. klinikum Carl Gustav Carus, Technische Universitat Dresden, Fetscherstrasse 74, D-01307 Dresden, Germany.
SOURCE: Nervenheilkunde, (2001) Vol. 20, No. 4, pp. 227-236.

Refs: 44
ISSN: 0722-1541 CODEN: NERVDI
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: German
SUMMARY LANGUAGE: English; German
ENTRY DATE: Entered STN: 28 Jun 2001
Last Updated on STN: 28 Jun 2001

AB Most of the commonly used antiparkinsonian drugs show neuroprotective potency when tested in tissue culture or animal models. Neuroprotection consists of measures which lead to prevention or delay of neuronal cell death. So far, there are no clinical studies which show undoubtably neuroprotection. Nonetheless, there are 3 PET- or SPECT-controlled studies with ropinirole, pergolide and promipexole finished which were designed to prove neuroprotection while taking dopamine agonists. This paper will further introduce studies with selegiline and NMDA receptor antagonists which indicate possible neuroprotection. Experimental data suggest studies with radical scavengers, coenzyme Q, iron chelators or antiapoptotic drugs such as flupirtine. Taking all consisting data into account we recommend to treat early Parkinsonism with a combination of selegiline, NMDA receptor antagonists and dopamine agonists.

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ACCESSION NUMBER: 2000395778 EMBASE
TITLE: [Akathisia secondary to tolcapone. Report of a case].
Acatisia secundaria a tolcapone. Reporte de un caso.
AUTHOR: Colorado-Ochoa, H. (correspondence)
CORPORATE SOURCE: Hospital ISSSTE, F. Magon 657-1 esq. de a llave, C.P. 91910
Veracruz Ver, Mexico.
SOURCE: Gaceta Medica de Mexico, (2000) Vol. 136, No. 5,
pp. 505-509.
Refs: 21
ISSN: 0016-3813 CODEN: GMMEAK
COUNTRY: Mexico
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: Spanish; Castilian
SUMMARY LANGUAGE: English; Spanish; Castilian
ENTRY DATE: Entered STN: 13 Dec 2000
Last Updated on STN: 13 Dec 2000

AB The purpose of this work is to report a case of tolcapone-induced akathisia. A 39-year-old woman with Parkinson's disease, Hohen-Yahr IV, Webster 18 points with 10 years within onset presented lack of clinical response to levodopa-carbidopa, pergolide, selegiline and trihexiphenidyl, showing freezing and wearing-off phenomena and choreic dyskinetic abnormal movements of the upper and lower extremities, during the six months previous to her evaluation. Her hepatic function was normal. Levodopa-carbidopa and selegiline were diminished to add tolcapone, as described elsewhere. During the first three weeks, the patient showed marked clinical improvement of previous complications and sustained improvement during 12.5 weeks. At the 13th week of tolcapone therapy the patient developed constant orofacial, trunk, and superior and lower limb involuntary movements associated to lack of stand still. Laboratory tests showed discrete elevation of oxaloacetic-glutamic transaminase, direct bilirubin, indirect bilirubin, and alkaline phosphatase. Electroencephalogram and

CT scan were normal. Tolcapone therapy was finished, and levodopacarbidopa, pergolide and selegiline were diminished, procuring the disappearance of akathisia within 72 h.

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ACCESSION NUMBER: 2000240718 EMBASE
TITLE: Entacapone and selegiline with L-dopa in patients with Parkinson's disease: An interaction study.
AUTHOR: Lyytinen, J. (correspondence); Kaakkola, S.; Teravainen, H.
CORPORATE SOURCE: Department of Neurology, University of Helsinki, Helsinki, Finland.
AUTHOR: Gordin, A.; Kultalahti, E.-R.
CORPORATE SOURCE: Orion Research Center, Orion Pharma, Espoo, Finland.
AUTHOR: Lyytinen, J. (correspondence)
CORPORATE SOURCE: Department of Neurology, University of Helsinki, PO Box 300, FIN-00039 Hyks, Finland.
SOURCE: Parkinsonism and Related Disorders, (Oct 2000)
Vol. 6, No. 4, pp. 215-222.
Refs: 26
ISSN: 1353-8020 CODEN: PRDIFO
PUBLISHER IDENT.: S 1353-8020(00)00012-2
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Jul 2000
Last Updated on STN: 20 Jul 2000

AB Both the catechol-O-methyltransferase (COMT) inhibitor entacapone and the monoamine oxidase B (MAO-B) inhibitor selegiline are L-dopa extenders. Both are used, often simultaneously, as adjuncts to L-dopa/dopa decarboxylase (DDC) inhibitor treatment of Parkinson's disease (PD). Their possible interactions have not been previously studied in a double-blind manner. We studied clinical response, tolerability, haemodynamics and cardiac rhythm in 16 PD patients with end-of-dose-type motor fluctuations. The patients' individual L-dopa/DDC inhibitor treatment was stabilized before the experimental treatments. This was followed by three consecutive, randomized, double-blind 2-week treatment periods with entacapone (200mg with each L-dopa dose), selegiline (10mg o.d.) or both entacapone and selegiline with the L-dopa/DDC inhibitor medication. Clinical efficacy (L-dopa test with repeated motor and dyskinesia scoring) and safety (orthostatic test, 24-h ambulatory ECG, haematological and clinical chemistry variables and adverse events) evaluations were performed before each treatment (control) and at the end of each treatment period. All three treatments, entacapone, selegiline, and entacapone+selegiline as adjunct to L-dopa/DDC inhibitor improved ($p < 0.05$) clinical disability compared to L-dopa only but they did not differ significantly from each other. Dyskinesias increased with all the treatments, statistically significantly ($p < 0.01$) with entacapone+selegiline. No significant differences in haemodynamics were observed between control and any of the experimental treatments, or between the experimental treatments in the orthostatic test. One patient already had symptomatic orthostatism before experimental treatments (control). In two other patients orthostatism emerged after the introduction of selegiline, and in one after every experimental treatment. Twenty-four-hour ECG did not show any differences in supraventricular or ventricular extrasystoles or heart rate between treatments. No statistically significant differences were

observed in adverse events or in haematology and clinical chemistry variables. One patient treated with entacapone+selegiline discontinued the study due to dizziness and insomnia. Our results suggest that co-administration of entacapone with L-dopa/DDC inhibitor, with or without selegiline, improves clinical disability, is safe, but may also enhance dopamine-related adverse events to some extent in PD patients with end-of-dose type motor fluctuations. Copyright (C) 2000 Elsevier Science Ltd.

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ACCESSION NUMBER: 2000067104 EMBASE
TITLE: Developments in the treatment of parkinson's disease.
SOURCE: Drug and Therapeutics Bulletin, (1999) Vol. 37,
No. 5, pp. 36-40.
Refs: 64
ISSN: 0012-6543 CODEN: DRTBAE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 2 Mar 2000
Last Updated on STN: 2 Mar 2000

AB Since we last reviewed the drug treatment of Parkinson's disease in 1995, several new drugs have been licensed for its treatment, more is known about the use of levodopa plus selegiline, and new surgical techniques have been developed. Here we review these new developments and consider how they affect patient management.

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ACCESSION NUMBER: 1999332535 EMBASE
TITLE: Parkinson's disease: Seven questions physicians often ask.
AUTHOR: Simuni, Tanya, Dr. (correspondence); Stern, Matthew B.
CORPORATE SOURCE: University of Pennsylvania.
AUTHOR: Simuni, Tanya, Dr. (correspondence); Stern, Matthew B.
CORPORATE SOURCE: Parkinson's Dis. Movement D., Pennsylvania Hospital, Univ. of Pennsylvania Health System, Philadelphia, PA, United States.
AUTHOR: Simuni, Tanya, Dr. (correspondence)
CORPORATE SOURCE: Parkinson's Dis./Movement Disorder, Center of Pennsylvania Hospital, Univ. of Pennsylvania Health System, Philadelphia, PA, United States.
SOURCE: Consultant, (Feb 1999) Vol. 39, No. 2, pp. 367-381.
Refs: 13
ISSN: 0010-7069 CODEN: CNSLAY
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
006 Internal Medicine
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 7 Oct 1999

Last Updated on STN: 7 Oct 1999

AB Parkinson's disease (PD) is a clinical diagnosis, based on the identification of parkinsonism, determination of its cause, and a positive clinical response to drug therapy. Six major groups of agents help control symptoms; levodopa, in combination with carbidopa, is the most effective, although each group of agents has a therapeutic niche. For example, dopamine agonists are somewhat less effective than levodopa, but are less likely to produce drug-induced dyskinesias; they also have a longer half-life than levodopa and provide steadier dopamine-receptor stimulation. Tokapone allows higher levels of levodopa to cross the blood-brain barrier without increasing the levodopa dose. Selegiline may help slow progression of early PD. The diagnosis of PD does not necessitate immediate drug therapy; start treatment when symptoms affect the patient's functional level. Surgery is reserved for patients who fail to benefit from medical therapy.

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ACCESSION NUMBER: 1999284654 EMBASE

TITLE: Medical and surgical treatment of Parkinson's disease: Strategies to slow symptom progression and improve quality of life.

AUTHOR: Conley, Scott C.; Kirchner, Jeffrey T. (correspondence)

CORPORATE SOURCE: ikirchner@desupernet.net

AUTHOR: Kirchner, Jeffrey T. (correspondence)

CORPORATE SOURCE: Dept. of Family/Community Medicine, Lancaster General Hospital, 555 N Duke St, Lancaster, PA 17604-3555, United States. ikirchner@desupernet.net

SOURCE: Postgraduate Medicine, (1999) Vol. 106, No. 2, pp. 41-52.

Refs: 18

ISSN: 0032-5481 CODEN: POMDAS

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 26 Aug 1999

Last Updated on STN: 26 Aug 1999

AB Despite new medical and surgical therapy, mortality rates for Parkinson's disease remain unchanged. Nevertheless, symptom progression can be slowed and quality of life improved with current methods of treatment. Levodopa is the most effective drug for Parkinson's disease, but its long-term use is associated with significant motor complications. Dopamine agonists hold promise because of more sustained stimulation of dopamine receptors and possibly an antioxidant effect. Selegiline, amantadine, and anticholinergics are still used but must be employed with caution in the elderly. COMT inhibitors may be useful adjuncts to levodopa therapy but are plagued with serious adverse effects. Goals of therapy in patients less than 60 years of age include sparing levodopa therapy and providing neuroprotection. For patients 60 years and older, goals include maintaining cognitive status and treating symptoms. Surgical treatment includes globus pallidus internal-segment pallidotomy, deep brain stimulation, and fetal nigral transplantation. These hold promise for the future.

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ACCESSION NUMBER: 1999280119 EMBASE

TITLE: Long term role of pergolide as an adjunct therapy
in Parkinson's disease: Influence on disability, blood
pressure, weight and levodopa syndrome.

AUTHOR: Sharma, J.C. (correspondence); Ross, I.N.

CORPORATE SOURCE: Newark Hospital, Newark, Nottinghamshire NG24 4DE, United
Kingdom. jsharma@lineone.net

SOURCE: Parkinsonism and Related Disorders, (Sep 1999)
Vol. 5, No. 3, pp. 111-114.
Refs: 15
ISSN: 1353-8020 CODEN: PRDIFO

PUBLISHER IDENT.: S 1353-8020(99)00017-6

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
006 Internal Medicine
008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 26 Aug 1999
Last Updated on STN: 26 Aug 1999

AB Pergolide is a dopamine agonist acting on D1 and D2 receptors
and has been used as an adjunct therapy with levodopa. We have
retrospectively investigated its role over a duration of upto six years in
Parkinson's disease (PD) patients to study: (1) its influence on
the progression of disability related to PD; (2) effect on blood pressure
and weight during the treatment period; (3) whether the use of
pergolide has a long term levodopa sparing effect; (4) and how is
it tolerated during this period? We studied 43 patients who had been on
adjunct therapy with pergolide in addition to levodopa for more
than six months. Mean age was 66 years, mean duration of PD prior to
adding pergolide was 8 years and final assessment was done after
a mean duration of adjunct therapy of 29 (6-72) months. There was no
progression of disease disability as assessed on Hoehn and Yahr stage ($p = 0.09$) and Webster score ($p = 0.20$), while there was an improvement in
symptom score ($p = 0.001$). There was an insignificant reduction in the
dose of levodopa at final assessment from 630 to 535 mg ($p = 0.06$). A
significant number of patients were able to discontinue taking
selegiline ($p = 0.002$). There was no change in the number of
patients with hallucinations ($p = 0.15$) and dyskinesia ($p = 0.09$). There
was a significant fall in weight ($p = 0.02$), systolic ($p = 0.023$) and
diastolic blood pressure ($p = 0.03$). This fall did not correlate with
age, dose of pergolide or levodopa or disease severity but was
influenced by duration of treatment. Ten patients discontinued
pergolide for minor reasons after a mean duration of therapy for
23 months. We conclude that pergolide is a valuable adjunct
therapy with levodopa over a duration of upto six years to maintain
control of motor symptoms of Parkinson's disease.

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ACCESSION NUMBER: 1999093317 EMBASE

TITLE: Management of early Parkinson's disease.

AUTHOR: Hauser, R.A., Dr. (correspondence); Zesiewicz, T.A.

CORPORATE SOURCE: Parkinson's Disease, Movement Disorders Center, 4 Columbia
Drive, Tampa, FL 33606, United States.

SOURCE: Medical Clinics of North America, (1999) Vol. 83,
No. 2, pp. 393-414.
Refs: 111
ISSN: 0025-7125 CODEN: MCNAA9

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
006 Internal Medicine
008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 1 Apr 1999

Last Updated on STN: 1 Apr 1999

AB The two major questions in the treatment of early PD are (1) Does selegiline slow neuronal loss and delay the progression of clinical disability? and (2) Should dopamine agonists be used as initial symptomatic therapy in early disease rather than levodopa/PDI to reduce long-term disability and delay the onset of motor fluctuations and dyskinesia? Selegiline affords neuroprotection for dopamine neurons in cell culture systems and the results of several clinical trials are consistent with the hypothesis that it is neuroprotective in Parkinson's disease. Several clinical trials have found that initial symptomatic therapy with dopamine agonist to which levodopa/carbidopa is later added when needed leads to a lower incidence of long-term motor complications. These strategies are now being tested in prospective, randomized, blinded trials, many of which include PET or SPECT scans to assess the rate of dopamine neuron loss. These trials will provide more definitive answers to guide the early medial management of Parkinson's disease in the future.

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ACCESSION NUMBER: 1998309383 EMBASE

TITLE: Pharmacoeconomic analysis of using Sinemet CR over standard Sinemet in Parkinsonian patients with motor fluctuations.

AUTHOR: Hempel, Alan G.

CORPORATE SOURCE: College of Pharmacy, Rutgers, State University of New Jersey, Piscataway, NJ, United States.

AUTHOR: Hempel, Alan G.

AUTHOR: Wagner, Mary L. (correspondence); Maaty, Mohamed A.

CORPORATE SOURCE: College of Pharmacy, Rutgers, State University of New Jersey.

AUTHOR: Maaty, Mohamed A.

AUTHOR: Sage, Jacob I.

CORPORATE SOURCE: Medical School, University of Medicine, Dentistry of New Jersey, New Brunswick, NJ, United States.

AUTHOR: Wagner, Mary L. (correspondence)

CORPORATE SOURCE: Department of Pharmacy Practice, College of Pharmacy, Rutgers, State University of New Jersey, 160 Frelinghuysen Rd., Piscataway, NJ 08854, United States.

AUTHOR: Wagner, Mary L. (correspondence)

CORPORATE SOURCE: Department of Pharmacy Practice, College of Pharmacy, State University of New Jersey, 160 Frelinghuysen Rd., Piscataway, NJ 08854, United States.

SOURCE: Annals of Pharmacotherapy, (Sep 1998) Vol. 32, No. 9, pp. 878-883.

Refs: 34

ISSN: 1060-0280 CODEN: APHRER

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 030 Clinical and Experimental Pharmacology

037 Drug Literature Index

008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English; French; Spanish; Castilian

ENTRY DATE: Entered STN: 9 Nov 1998

Last Updated on STN: 9 Nov 1998

AB OBJECTIVE: To compare the costs of pharmacotherapy in patients with Parkinson's disease before and after converting from standard Sinemet to extended-release Sinemet CR. DESIGN: Investigators retrospectively reviewed records of patients converting from Sinemet to Sinemet CR for efficacy and total drug costs. Cost-effectiveness was evaluated retrospectively from data collected in prospective Sinemet CR efficacy trials. SETTING: Parkinson's disease clinic at a tertiary care university teaching hospital. PATIENTS: 100 patients with motor fluctuations who had undergone an initial 6-month course of Sinemet therapy, followed by a 6-month course of Sinemet CR. MAIN OUTCOME MEASURES: Total cost was measured as the cost of Sinemet formulations plus the costs of other antiparkinson medications. Differences in pre- and postconversion costs were compared by using the paired, two-tailed Student's t-test. A substudy of 39 patients on the cost-effectiveness of conversion measured the ratio of daily medication costs to the daily hours 'on' without chorea. RESULTS: While total daily medication costs after conversion increased by 21%, patients experienced either a comparable or an improved degree of disease control with Sinemet CR. Patients who were also taking selegiline were able to decrease selegiline expense by 20%. The costs of other adjunctive medications did not differ significantly after conversion. The cost-effectiveness analysis revealed an increase in postconversion on time by 2.2 hours ($p = 0.0001$), accompanied by a \$2.85 decrease in total cost per hour on without chorea ($p = 0.11$). CONCLUSIONS: Although Sinemet CR is more costly, it may be more cost-effective in patients with motor fluctuations. Some patients may be able to reduce adjunctive medications.

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ACCESSION NUMBER: 1998284119 EMBASE
TITLE: Advances in Parkinson's disease treatment.
AUTHOR: Pittman, J.R. (correspondence); Rogers, C.M.
CORPORATE SOURCE: School of Pharmacy, University of Mississippi, Mississippi, MS, United States.
SOURCE: Drug Topics, (3 Aug 1998) Vol. 142, No. 15, pp. 52-59.
ISSN: 0012-6616 CODEN: DGTNA7
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 Oct 1998
Last Updated on STN: 9 Oct 1998

AB More pharmacologic treatments for symptomatic management of Parkinson's disease are available, but several controversies exist as to which medications should be used as monotherapy in early treatment. While levodopa remains the mainstay of treatment, controversy exists regarding the formation of hydroxy radicals as a byproduct of levodopa metabolism, which may increase dopaminergic neuron destruction. Dopamine agonists have been shown to delay levodopa use. Selegiline improves symptoms; however, clinical trials have not proven that it has any neuroprotective role. The COMT inhibitors, in combination with carbidopa/levodopa, provide new options for managing advanced-disease patients with dyskinesias and motor fluctuations. Patient education and nonpharmacologic interventions also play an important therapeutic role.

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ACCESSION NUMBER: 1998195943 EMBASE
 TITLE: Initiating therapy for Parkinson's disease.
 AUTHOR: Silver, Dee E., Dr. (correspondence)
 CORPORATE SOURCE: Scripps Memorial Hospital, San Diego, CA, United States.
 AUTHOR: Ruggieri, Stefano
 CORPORATE SOURCE: Dipartimento di Scienze Neurologiche, Universita La Sapienza, Rome, Italy.
 AUTHOR: Ruggieri, Stefano
 CORPORATE SOURCE: IRCCS Neuromed, Pozzilli, Italy.
 AUTHOR: Silver, Dee E., Dr. (correspondence)
 CORPORATE SOURCE: 9850 Genesee Ave., San Diego, CA 92037, United States.
 AUTHOR: Silver, Dee E., Dr. (correspondence)
 CORPORATE SOURCE: 9850 Genesee Ave., San Diego, CA 92037, United States.
 SOURCE: Neurology, (Jun 1998) Vol. 50, No. 6 SUPPL.6, pp. S18-S22.
 Refs: 22
 ISSN: 0028-3878 CODEN: NEURAI
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 008 Neurology and Neurosurgery
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 20 Aug 1998
 Last Updated on STN: 20 Aug 1998

AB Accurate diagnosis and individualized assessment of the risks and benefits of available antiparkinsonian medications should guide initiation of treatment for patients with early Parkinson's disease (PD). In general, the goals of treatment for younger patients (less than age 60 years) are control of impairing symptoms, sparing of levodopa to minimize long-term complications, and consideration of neuroprotection. The primary initial medication choices for patients under age 50 years include selegiline, amantadine, and anticholinergic agents. Patients in their fifties may require a dopamine agonist in addition to or instead of selegiline to achieve adequate symptom control. If the desired response is still not achieved, sustained-release carbidopa-levodopa should be added, followed by adjunctive amantadine or anticholinergic therapy. For older patients (60 years and over), improvement of functional impairment is the primary goal. For these patients, a special concern is to avoid inducing or exacerbating cognitive impairment. Sustained-release carbidopa-levodopa is considered first-line treatment for these patients. Inadequate response can be handled by a trial of immediate-release carbidopa-levodopa and then addition of a dopamine agonist when maximum levodopa doses are reached. Anticholinergic agents, amantadine, and selegiline should be avoided because of their CNS effects.

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ACCESSION NUMBER: 1998158429 EMBASE
 TITLE: Medical treatment of essential tremor and Parkinson's disease.
 AUTHOR: Uitti, Ryan J., Dr. (correspondence)
 CORPORATE SOURCE: Department of Neurology, Mayo Medical School, Jacksonville, FL, United States.
 AUTHOR: Uitti, Ryan J., Dr. (correspondence)
 CORPORATE SOURCE: Department of Neurology, Movement Disorders Division, Mayo Clinic, Jacksonville, FL, United States.
 SOURCE: Geriatrics, (May 1998) Vol. 53, No. 5, pp. 46-57.
 Refs: 14

ISSN: 0016-867X CODEN: GERIAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 020 Gerontology and Geriatrics
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 18 Jun 1998
Last Updated on STN: 18 Jun 1998

AB Although there is no known cure for essential tremor or Parkinson's disease (PD), medical treatment can often significantly reduce or eliminate functional disability. Mild essential tremor does not require treatment, and early treatment does not arrest or slow the natural progression in symptoms. When essential tremor interferes with daily activities, medical treatment options include beta blockers, anticonvulsants, benzodiazepines, and carbonic anhydrase inhibitors. Because of the great variability in the presentation of PD, no single approach is appropriate for all patients. Levodopa is the mainstay of pharmacologic therapy for PD, although other agents are indicated for monotherapy or in combination with levodopa. These include traditional and newer dopamine agonists, amantadine, anticholinergics, selegiline, and an emerging class of agents called COMT inhibitors.

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ACCESSION NUMBER: 1998003082 EMBASE
TITLE: Parkinson's disease: Drug therapy.
AUTHOR: Oertel, W.H., Dr. (correspondence); Quinn, N.P.
CORPORATE SOURCE: Philipps-Universitat Marburg, Klinik fur Neurologie, Zentrum fur Nervenheilkunde, Rudolf-Bultmann Strasse 8, D-35033 Marburg, Germany.
SOURCE: Bailliere's Clinical Neurology, (1997) Vol. 6, No. 1, pp. 89-108.
Refs: 84

ISSN: 0961-0421 CODEN: BCNUEK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
006 Internal Medicine
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 22 Jan 1998
Last Updated on STN: 22 Jan 1998

AB Unlike the situation in patients with most other degenerative neurological disorders, individuals with Parkinson's disease (PD) and their physicians have a wide range of effective symptomatic drugs at their disposal. All have somewhat differing indications, potencies and side-effects, and treatment needs to be individualized and also altered as the disease and the duration of drug treatment progress and the patient ages. The main problem for most patients after prolonged treatment with L-dopa is the long-term L-dopa syndrome. Fluctuations and dyskinesias are usually the principal complaint in younger, and neuropsychiatric symptoms in older, patients. Although L-dopa is the 'gold standard' in terms of efficacy, these treatment-related problems make it necessary to regularly monitor patients' response to treatment and if necessary to modify their drug regime accordingly and, particularly in younger patients, to devise treatment strategies whereby the use of L-dopa can be limited or delayed. Currently available alternative or adjunctive treatments to L-dopa

preparations include oral dopamine agonists, subcutaneous apomorphine, amantadine, selegiline and anticholinergics, and some guidelines about how and when to use all of these drugs or classes of drugs are presented in this chapter. Despite initial claims of neuroprotection by selegiline, we are still awaiting the more promising second era of drug treatment for PD, whereby hopefully we can retard, halt or prevent the disease itself.

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ACCESSION NUMBER: 1997225143 EMBASE
TITLE: [Parkinson's disease. Pharmacotherapy, insights and advances].
Farmacotherapie, inzichten en ontwikkelingen. Ziekte van Parkinson.
AUTHOR: Esselink, R.A.J.
CORPORATE SOURCE: Rijksuniversiteit Groningen.
AUTHOR: Jansen, E.N.H.
AUTHOR: Jansen Steur, E.N.H., Dr. (correspondence)
CORPORATE SOURCE: Afdeling Neurologie, Movement Disorder Unit, Medisch Spectrum Twente, Postbus 50.000, 7500 KA Enschede, Netherlands.
SOURCE: Pharmaceutisch Weekblad, (1 Aug 1997) Vol. 132, No. 31, pp. 1144-1151.
Refs: 54
ISSN: 0031-6911 CODEN: PHWEAW
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: Dutch; Flemish
SUMMARY LANGUAGE: Dutch; Flemish; English
ENTRY DATE: Entered STN: 4 Sep 1997
Last Updated on STN: 4 Sep 1997

AB In Parkinson's disease, clinically characterized by tremor, rigidity, bradykinesia and impaired postural reflexes, a dopamine depletion in the nigrostriatal system is present. The neuropathological hallmarks are Lewy bodies in the substantia nigra, other brainstem nuclei, and cerebral cortex. Parkinson's disease is often associated with cognitive decline and depressive symptoms. Potential etiologies are exogenous neurotoxins, apoptosis, genetic factors, and oxidative stress. Drug therapy exists of anticholinergics, amantadine, levodopa, dopamine agonists, selegiline (dopamine agonistic and neuroprotective effects), clozapine, in the near future COMT inhibitors, or combinations of these drugs. Surgical interventions mentioned are chronic stimulation or lesioning of the thalamus or globus pallidus and possibly in the future brain grafting. Glutamate antagonists and 'nerve growth factors' may be future therapies; they might prevent further degeneration or even stimulate the function of surviving neurons.

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ACCESSION NUMBER: 1997187973 EMBASE
TITLE: Pharmacologic options for managing Parkinson's disease.
AUTHOR: Evidente, Virgilio G. H.
CORPORATE SOURCE: Mayo Clinic, Scottsdale, AZ, United States.
AUTHOR: Adler, Charles H., Dr. (correspondence)
CORPORATE SOURCE: Parkinson's Dis. Movement Disord. C., Department of Neurology, Mayo Clinic, Scottsdale, AZ, United States.
AUTHOR: Adler, Charles H., Dr. (correspondence)
CORPORATE SOURCE: Department of Neurology, Mayo Clinic Scottsdale, 13400 Shea Blvd., Scottsdale, AZ 85259, United States.

SOURCE: Formulary, (Jun 1997) Vol. 32, No. 6, pp.
594-596+601-602+604+607-610.

Refs: 54

ISSN: 0098-6909 CODEN: FORMF9

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 037 Drug Literature Index

008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 31 Jul 1997

Last Updated on STN: 31 Jul 1997

AB Current therapy for idiopathic Parkinson's disease (IPD) is mainly symptomatic with the focus on individualizing therapy for early and advanced stage disease. The most effective drug for both early and advanced IPD is levodopa. For patients with mild disease and minimal disability, monotherapy with anticholinergic agents, amantadine, selegiline, or dopamine agonists (eg, bromocriptine and pergolide) may be useful. Advanced disease is usually associated with levodopa-induced complications, such as motor fluctuations and dyskinesias, which may be alleviated by adjusting levodopa dosing or by adding a dopamine agonist. Although no drug has been unequivocally proven to be neuroprotective in IPD, selegiline, amantadine, bromocriptine, and pergolide may play some role in delaying the progression of disease.

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ACCESSION NUMBER: 1996251706 EMBASE

TITLE: Controversies in the treatment of Parkinson's disease.

AUTHOR: Hely, Mariese A.; Morris, John G.L. (correspondence)

CORPORATE SOURCE: Department of Neurology, Westmead Hospital, Sydney, NSW 2145, Australia.

SOURCE: Current Opinion in Neurology, (1996) Vol. 9, No. 4, pp. 308-313.

Refs: 43

ISSN: 1350-7540 CODEN: CONEEX

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 037 Drug Literature Index

038 Adverse Reactions Titles

008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 17 Sep 1996

Last Updated on STN: 17 Sep 1996

AB Although theoretical reasons exist for believing that selegiline slows the progression of Parkinson's disease, this has not been shown in clinical trials. Selegiline improves the symptoms of Parkinson's disease, allowing the introduction of levodopa to be delayed in de-novo patients and, later, for levodopa to be used at a lower dose. It does not lessen the long-term problems of dyskinesia and fluctuations associated with levodopa therapy. The report of an increased mortality associated with selegiline therapy awaits further evaluation. Of the dopamine agonists, pergolide appears to be more potent than bromocriptine; cabergoline looks promising. The catechol-O-methyltransferase inhibitors, tolcapone and entacapone, prolong the duration of action of levodopa and also show promise. The main objective in the drug treatment of Parkinson's disease remains the optimization of the dose and frequency of levodopa administration.

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ACCESSION NUMBER: 1996028119 EMBASE
TITLE: Moderate Parkinson's disease: Strategies for maximizing treatment.
AUTHOR: Silverstein, P.M., Dr. (correspondence)
CORPORATE SOURCE: Minneapolis Clinic of Neurology, Ltd, W-414 Meadowbrook Medical Building, 6490 Excelsior Blvd, St Louis Park, MN 55426-4710, United States.
SOURCE: Postgraduate Medicine, (1996) Vol. 99, No. 1, pp. 52-54+61-63+67-68.
ISSN: 0032-5481 CODEN: POMDAS
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 6 Feb 1996
Last Updated on STN: 6 Feb 1996

AB Motor fluctuations and dyskinesia often develop in patients with Parkinson's disease after 3 to 5 years of levodopa therapy. Dosage adjustments, addition of a second medication to the drug regimen, and dietary modifications may help maximize response to symptomatic therapy. Given the dramatic variability of symptoms and response to treatment, drug regimens must be individualized according to the patient's needs. In newly diagnosed cases of Parkinson's disease, administration of selegiline hydrochloride (Eldepryl) may slow symptom development and delay the need for levodopa therapy. Many physicians prescribe selegiline initially for its symptomatic and potential neuroprotective benefits.

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ACCESSION NUMBER: 1995302698 EMBASE
TITLE: Selegiline reduces need for levodopa in Parkinson's disease.
SOURCE: Drugs and Therapy Perspectives, (1995) Vol. 6, No. 8, pp. 5-8.
ISSN: 1172-0360 CODEN: DTHPEE
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 Nov 1995
Last Updated on STN: 11 Nov 1995

AB The selective monoamine oxidase type B inhibitor selegiline has a role in patients with early Parkinson's disease and in selected patients with suboptimal responses to levodopa. When selegiline is used as monotherapy in early disease, the onset of symptoms severe enough to warrant levodopa therapy may be delayed to 6 to 9 months. In patients who require levodopa therapy, but experience either a suboptimal peak response or end of dose 'wearing off' effects, the addition of selegiline may improve motor function and be levodopa-sparing. Whether the beneficial effects of selegiline arise from neuroprotection or are purely symptomatic remains controversial.

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ACCESSION NUMBER: 1995243051 EMBASE
TITLE: The therapeutic potential of moclobemide, a reversible selective monoamine oxidase A inhibitor in Parkinson's disease.
AUTHOR: Sieradzan, K., Dr. (correspondence); Channon, S.; Ramponi, C.; Stern, G.M.; Lees, A.J.; Youdim, M.B.H.
CORPORATE SOURCE: Department of Neurology, Manchester Royal Infirmary, Oxford Road, Manchester M13, United Kingdom.
SOURCE: Journal of Clinical Psychopharmacology, (1995) Vol. 15, No. 4 SUPPL. 2, pp. 51S-59S. ISSN: 0271-0749 CODEN: JCPYDR
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 020 Gerontology and Geriatrics
030 Clinical and Experimental Pharmacology
032 Psychiatry
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 6 Sep 1995
Last Updated on STN: 6 Sep 1995

AB Dopamine is equally well deaminated oxidatively by monoamine oxidase (MAO) A and B types. Selegiline (L-deprenyl), a selective inhibitor of MAO-B, ameliorates the 'wearing off' akinesia and delays the need for levodopa in mild, previously untreated Parkinson's disease. The therapeutic potential of selective inhibition of MAO-A in Parkinson's disease has not been examined in detail. MAO-A accounts for only about 20% Of total MAO activity in the human basal ganglia, and it differs from MAO-B in distribution. In contrast to MAO-B, which is confined to the extraneuronal compartment, MAO-A is found both extraneuronally and within the presynaptic dopaminergic terminals. The inhibition of MAO-A might alter the intraneuronal handling of dopamine reuptaken from synaptic clefts and thereby prolong oral levodopa benefit. We have given moclobemide, a selective, reversible inhibitor of MAO-A, to nondepressed patients with Parkinson's disease receiving standard levodopa/peripheral decarboxylase inhibitor or levodopa with dopaminergic agonist (bromocriptine, pergolide). Selegiline was discontinued at least 8 weeks earlier. A standard oral levodopa challenge was performed at the patient's entry to the; study and repeated on the 22nd day of moclobemide treatment (150 mg thrice daily). The overall timespent 'on' and 'off' before the onset of treatment and during the last week on the drug was estimated from the patients' diaries. Neuropsychological assessments were also made before and after 3 weeks of moclobemide to measure possible effects on cognitive performance and mood. In acute levodopa challenge, the latency of motor response was significantly shortened and its duration was prolonged during moclobemide treatment. Similarly, the Webster's scores in 'off' state after overnight withdrawal of dopaminergic medication improved on moclobemide. In nondepressed parkinsonian patients, moclobemide did not alter mood and cognitive measures. The mild symptomatic effect and good tolerance with standard therapy suggest that moclobemide may be a particularly useful antidepressant in Parkinson's disease.

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ACCESSION NUMBER: 1994376272 EMBASE
TITLE: Early idiopathic parkinsonism: Initiation and optimization of treatment.

AUTHOR: Calne, D.B., Dr. (correspondence)
 CORPORATE SOURCE: Neurodegenerative Disorders Centre, Faculty of Medicine,
 Vancouver Hospital, Vancouver, BC V6T 2B5, Canada.
 SOURCE: Clinical Neuropharmacology, (1994) Vol. 17, No.
 SUPPL. 2, pp. S14-S18.
 ISSN: 0362-5664 CODEN: CLNEDB
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
 FILE SEGMENT: 037 Drug Literature Index
 038 Adverse Reactions Titles
 008 Neurology and Neurosurgery
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 18 Jan 1995
 Last Updated on STN: 18 Jan 1995

AB Once a diagnosis of idiopathic parkinsonism has been made, the choice and timing of therapy depend almost entirely on the patient's need for symptomatic relief, as no presently available therapy has any effect on the pathogenesis of the disease. Five categories of drugs are available for the treatment of idiopathic parkinsonism. Anticholinergic agents are effective against tremor but have prominent adverse effects. Amantadine has similar effects but is more active against rigidity and bradykinesia. Selegiline is a monoamine oxidase-B inhibitor; once thought to affect the pathogenesis of idiopathic parkinsonism, it is now known to offer only symptomatic relief. The dopamine agonists (bromocriptine, pergolide, and lisuride) stimulate D(2) receptors; they have antiparkinsonian effects and tolerance profiles broadly similar to those of levodopa but are slightly less efficacious. Pleural effusions and pulmonary fibrosis are unusual but important complications of these drugs; chest x-ray examinations are therefore recommended for all patients starting such treatment. Levodopa (combined with an extracerebral decarboxylase inhibitor to prevent nausea, the main adverse effect) has become the standard antiparkinsonism treatment. Patients using this preparation can suffer considerable variations in mobility and dyskinesia, which may be related to rapid, large-scale oscillations in plasma levodopa concentrations. Controlled-release (CR) preparations have been developed in an attempt to minimize these fluctuations and reduce long-term side effects. There is no universally agreed treatment for idiopathic parkinsonism. However, experience shows that a good balance of antiparkinsonian activity and adverse effects can be obtained by initiating treatment with a combination of levodopa and a decarboxylase inhibitor. A dopamine agonist can be added if the disease progresses and increased therapeutic activity is required.

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ACCESSION NUMBER: 1994119237 EMBASE
 TITLE: Treatment of Parkinson's disease: From theory to practice.
 AUTHOR: Ahlskog, J.E., Dr. (correspondence)
 CORPORATE SOURCE: Department of Neurology, Mayo Clinic, Rochester, MN 55905,
 United States.
 SOURCE: Postgraduate Medicine, (1994) Vol. 95, No. 5, pp.
 52-54+57-58+61-64+68-69.
 ISSN: 0032-5481 CODEN: POMDAS
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
 FILE SEGMENT: 037 Drug Literature Index
 008 Neurology and Neurosurgery
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 11 May 1994

Last Updated on STN: 11 May 1994

AB Parkinson's disease responds rather dramatically to levodopa therapy during the first several years of treatment. With advancing disease, however, symptom control becomes more erratic, and some symptoms may become refractory to treatment. The use of selegiline hydrochloride (Eldepryl) has been proposed to slow the progression of Parkinson's disease; however, current evidence suggests that it is only partially effective at best, and there is no definite proof of a neuroprotective effect. Nonetheless, it is a reasonable treatment choice. Carbidopa-levodopa (Sinemet) remains the foundation of symptomatic treatment of Parkinson's disease. Clinical fluctuations occurring with advancing disease may be at least partially controlled by appropriate adjustments in dosage. A direct-acting dopamine agonist, bromocriptine mesylate (Parlodel) or pergolide mesylate (Permax), can be very helpful as adjunctive therapy to smooth these clinical fluctuations. Excessive intracellular oxidative stress has been proposed as a cause of Parkinson's disease; however, a recent multicenter trial investigating the use of high doses of the antioxidant vitamin E showed it to be ineffective. Whether other forms of nonspecific antioxidant therapy will prove beneficial is open to speculation.

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ACCESSION NUMBER: 1993251624 EMBASE
TITLE: Strategies in the treatment of early Parkinson's disease.
AUTHOR: Rinne, U.K. (correspondence)
CORPORATE SOURCE: Department of Neurology, University of Turku, SF-20520 Turku, Finland.
SOURCE: Acta Neurologica Scandinavica, Supplement, (1993)
Vol. 87, No. 146, pp. 50-53.
ISSN: 0065-1427 CODEN: ANSLAC
COUNTRY: Denmark
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 26 Sep 1993
Last Updated on STN: 26 Sep 1993

AB Over recent years I have been studying whether dopamine agonist treatment alone, or in early combination with levodopa, might institute a better long- term treatment in Parkinson's disease than levodopa alone. Indeed, early combination of levodopa with bromocriptine, pergolide or lisuride has indicated that this kind of treatment results in better management of Parkinson's disease with fewer fluctuations in disability, especially end- of-dose disturbances and dyskinesias, than treatment with levodopa alone. Furthermore, similar results were obtained by using lisuride in combination with selegiline and levodopa. Thus, it appears advisable to initiate the dopaminergic treatment in early Parkinson's disease by using a combination of selegiline, levodopa and a dopamine agonist. There are many ways of building up this kind of treatment. Instead of levodopa, it is possible to use initially a dopamine agonist and to add selegiline and levodopa when the therapeutic response becomes insufficient. Another alternative would be to start with selegiline alone, then to add a dopamine agonist and, finally, levodopa when clinically indicated.

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ACCESSION NUMBER: 1993165872 EMBASE
TITLE: Treatment of Parkinson's disease.

AUTHOR: Lieberman, A. (correspondence)
CORPORATE SOURCE: Movement Disorders, Barrow Neurological Institute, St Joseph's Medical Center, 350 West Thomas Road, Phoenix, AZ 85013, United States.
SOURCE: Current Opinion in Neurology and Neurosurgery, (1993) Vol. 6, No. 3, pp. 339-343.
ISSN: 0951-7383 CODEN: CNENE8
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jul 1993
Last Updated on STN: 4 Jul 1993

AB The treatment of Parkinson's disease is reviewed. The rationale for using selegiline (deprenyl) as the first treatment in recently diagnosed patients is presented. Selegiline delays the need for levodopa; however, it is unclear whether this results from a symptomatic or a neuroprotective effect of selegiline. Levodopa combined with a decarboxylase inhibitor is the principal treatment for patients with moderate or marked symptoms. There is little evidence that levodopa has a deleterious effect on the course of Parkinson's disease. The relationship of levodopa to dyskinesias and response fluctuations is discussed. Pharmacokinetic and pharmacodynamic studies suggest that continuous dopaminergic stimulation may be superior to intermittent pulse therapy. The best approximation to continuous stimulation is the use of long-acting levodopa-carbidopa preparations supplemented by dopamine agonists.

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ACCESSION NUMBER: 1993086344 EMBASE
TITLE: Management of the patient with newly-diagnosed Parkinson's disease.
AUTHOR: Paulson, G.W., Prof. (correspondence)
CORPORATE SOURCE: Department of Neurology, Ohio State University, Columbus, OH, United States.
SOURCE: Geriatrics, (1993) Vol. 48, No. 2, pp. 30-34+39-40.
ISSN: 0016-867X CODEN: GERIAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 020 Gerontology and Geriatrics
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 25 Apr 1993
Last Updated on STN: 25 Apr 1993

AB Initial therapy of a patient newly diagnosed with Parkinson's disease depends on a variety of presenting symptoms and therefore must be individualized. Some patients do not initially require any therapy or can be managed with small doses of antidepressants. Anticholinergics are useful initial drugs for some patients, particularly when tremor is a presenting symptom. For rigidity, levodopa is the drug most likely to be helpful. Dopamine agonists and amantadine may be used initially, but more often are used as adjunct therapy later in the course of the disease. Selegiline probably should be considered for all newly diagnosed patients, because it may have the potential to slow disease progression.

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ACCESSION NUMBER: 1993082710 EMBASE
TITLE: Parkinson's disease and the elderly patient.
AUTHOR: Oles, K.S., Prof. (correspondence)
CORPORATE SOURCE: Department of Neurology, Northwest Area Health Educ Center, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, NC 27103, United States.
SOURCE: Journal of Geriatric Drug Therapy, (1992) Vol. 6, No. 4, pp. 41-71.
ISSN: 8756-4629 CODEN: JGDTEF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 020 Gerontology and Geriatrics
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 18 Apr 1993
Last Updated on STN: 18 Apr 1993

AB Parkinson's disease affects 1-3% of the elderly. It is associated with disabilities that may be confused with other common problems of aging, such as gait disturbances, postural hypotension, constipation, dementia, depression, urinary dysfunction, sensory changes, pain and stiffness and tremor. Swallowing difficulties may make oral drug consumption difficult. Drug-induced parkinsonism is more common and often irreversible in elderly patients. Pharmacokinetic changes in the elderly and dosage recommendations are reviewed. Controlled clinical trials comparing single drugs or combinations are unusual in Parkinson's disease and none exist for the most elderly. Side effects, such as cognitive dysfunction from anticholinergic medications, psychiatric side effects and postural hypotension are more common in the elderly; response fluctuations while on levodopa are less apparent in the aged. Selegiline has a good side effect profile. Its long-term efficacy may be better than that of low-dose dopamine agonists. It appears to delay the necessity for levodopa treatment in some patients. Selegiline may be considered a drug of choice in Stages I and II and as an adjunct to levodopa in more advanced Parkinson's disease. A flexible, individualized approach using objective therapeutic endpoints will optimize treatment.

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ACCESSION NUMBER: 1992234837 EMBASE
TITLE: [Drug treatment in Parkinson's disease].
DE MEDICAMENTEUZE BEHANDELING VAN DE ZIEKTE VAN PARKINSON.
AUTHOR: Hovestadt, A., Dr. (correspondence)
CORPORATE SOURCE: Ziekenhuis Eemland, Utrechtseweg 160, 3818 ES Amersfoort, Netherlands.
SOURCE: TGO - Tijdschrift voor Therapie Geneesmiddel en Onderzoek, (1992) Vol. 17, No. 5, pp. 147-151.
ISSN: 0921-562X CODEN: TTTOE9
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: Dutch; Flemish
SUMMARY LANGUAGE: Dutch; Flemish; English
ENTRY DATE: Entered STN: 30 Aug 1992
Last Updated on STN: 30 Aug 1992

AB Parkinson's disease can initially be treated with

selegiline (10 mg daily dose) in the assumption that selegiline retards the progression of the disease. Should symptomatic therapy be required, amantadine or anticholinergics can be prescribed, possibly in combination. When progression occurs, and certainly with the appearance of postural instability, levodopa-substitution-therapy should be instituted. At later stages dopamine-agonists can be added. In this phase treatment should be supervised by a neurologist.

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ACCESSION NUMBER: 1992220629 EMBASE
TITLE: Update on drug treatments for Parkinson's disease.
AUTHOR: Swanson, P.D., Dr. (correspondence)
CORPORATE SOURCE: Division of Neurology, Department of Medicine, University of Washington, Seattle, WA, United States.
SOURCE: Drug Therapy, (1992) Vol. 22, No. 6, pp. 89-95.
ISSN: 0001-7094 CODEN: DRTHE2
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Aug 1992
Last Updated on STN: 16 Aug 1992

AB The number of drugs available for treating Parkinson's disease is increasing. The most effective drug remains Sinemet, which combines the peripheral decarboxylase inhibitor carbidopa with levodopa. Two dopamine agonists, one monoamine oxidase B inhibitor (selegiline), and several other agents, most of them anticholinergics, have adjunctive roles in treating parkinsonian symptoms. It is hoped that selegiline slows the progression of the disease, but this hypothesis has not been proved.

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ACCESSION NUMBER: 1992118764 EMBASE
TITLE: The place of the dopaminergic agonists in the treatment of Parkinson's disease: The view from the trenches.
AUTHOR: King, D.B. (correspondence)
CORPORATE SOURCE: 1030 South Park Street, Halifax, NS B3H 2S3, Canada.
SOURCE: Canadian Journal of Neurological Sciences, (1992)
Vol. 19, No. 1 SUPPL., pp. 156-159.
ISSN: 0317-1671 CODEN: CJNSA2
COUNTRY: Canada
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 15 May 1992
Last Updated on STN: 15 May 1992

AB The use of the dopamine receptor agonists in Parkinson's disease has a compelling logic. These agents are supposed to act independently of the dying cells of the substantia nigra directly on the cells of the striatum. Early clinical trials in advanced disease were only mildly impressive. Later they were found to be beneficial in early disease but their effectiveness waned. Their ultimate failure may reflect the fact that the majority of current agents do not stimulate D1 and D2 receptors in a physiologic ratio. The drugs may act presynaptically and with the

eventual loss of the anatomic relationships between nigra and striatum the drugs fail. There is, however, a rationale to their current use. When used along with L-Dopa in early disease the development of late-stage fluctuations are reduced with the same anti-parkinsonian benefits. Merging this concept with the demonstrated effect of selegiline in slowing the course of the disease, the current practice of triple therapy with selegiline, L-Dopa and a dopamine receptor agonist emerges.

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ACCESSION NUMBER: 1992116942 EMBASE
TITLE: Parkinson's disease: Update on pharmacologic options to slow progression and treat symptoms.
AUTHOR: Ahlskog, J.E.
SOURCE: Hospital Formulary, (1992) Vol. 27, No. 2, pp. 146-163.
ISSN: 0098-6909 CODEN: HOFOD9
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 15 May 1992
Last Updated on STN: 15 May 1992

AB Medical treatment of Parkinson's disease is becoming increasingly complex. Carbidopa/levodopa continues to be the most efficacious medication available. Other recent evidence suggests that selegiline might slow Parkinson's disease progression. The direct-acting dopamine agonists, bromocriptine and pergolide, are often beneficial in patients with short-duration, fluctuating levodopa responses. These medications have also been advocated for initial symptomatic treatment, concurrent with the initiation of carbidopa/levodopa; however, this use is controversial. The controlled-release formulation of carbidopa/levodopa typically prolongs the levodopa response by approximately 30%, but some patients prefer the standard formulation due to its faster onset of action. The expense of using two or more of these medications is of concern to this patient population.

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ACCESSION NUMBER: 1992056315 EMBASE
TITLE: Newly-diagnosed Parkinson's disease: A therapeutic update.
AUTHOR: Pleet, A.B.
CORPORATE SOURCE: Tufts University School of Medicine, Boston, MA, United States.
SOURCE: Geriatrics, (1992) Vol. 47, No. 1, pp. 24-29.
ISSN: 0016-867X CODEN: GERIAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 020 Gerontology and Geriatrics
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Mar 1992
Last Updated on STN: 29 Mar 1992

AB For patients with newly-diagnosed Parkinson's disease, current research is pointing to new therapeutic approaches. Those that are now

available allow the institution of levodopa to be delayed until there is some functional disability requiring treatment. Treating mild symptoms with anticholinergics and other agents may delay the use of levodopa for up to 3 years. And when finally required, levodopa may be used at lower doses when combined with carbidopa and a dopamine agonist. The monoamine oxidase type B inhibitor selegiline is also being used by many physicians to delay the onset of disability.

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ACCESSION NUMBER: 1992035022 EMBASE
TITLE: New strategies in the treatment of early Parkinson's disease.
AUTHOR: Rinne, U.K. (correspondence)
CORPORATE SOURCE: Department of Neurology, University of Turku, SF-20520 Turku, Finland.
SOURCE: Acta Neurologica Scandinavica, Supplement, (1991) Vol. 84, No. 136, pp. 95-98.
ISSN: 0065-1427 CODEN: ANSLAC
COUNTRY: Denmark
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Mar 1992
Last Updated on STN: 20 Mar 1992

AB Over recent years I have been studying whether dopamine agonist treatment alone, or in early combination with levodopa, might institute a better long-term treatment in Parkinson's disease than levodopa alone. Indeed, early combination of levodopa with bromocriptine, pergolide or lisuride has indicated that this kind of treatment results in better management of Parkinson's disease with fewer fluctuations in disability, especially end-of-dose disturbances and dyskinesias, than treatment with levodopa alone. Furthermore, similar results were obtained by using lisuride in combination with selegiline and levodopa. However, during long-term treatment the changes in parkinsonian disability were equal in all treatment groups with or without selegiline. Thus, the possible efficacy of selegiline in slowing down the progression of Parkinson's disease requires further investigations. As a new treatment strategy it appears advisable to initiate the dopaminergic treatment in early Parkinson's disease by using initially selegiline and a dopamine agonist and by adding levodopa when the therapeutic response is insufficient. Another alternative would be to start with selegiline alone, then add a dopamine agonist and, finally, levodopa.

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ACCESSION NUMBER: 1991259533 EMBASE
TITLE: Behavioral complications of drug treatment of Parkinson's disease.
AUTHOR: Cummings, J.L.
CORPORATE SOURCE: Neurobehavior Unit, West LA VAMC, 11301 Wilshire Blvd., Los Angeles, CA 90073, United States.
AUTHOR: Cummings, J., Dr. (correspondence)
CORPORATE SOURCE: Neurobehavior Unit, West LA VAMC, 11301 Wilshire Blvd., Los Angeles, CA 90073, United States.
SOURCE: Journal of the American Geriatrics Society, (1991) Vol. 39, No. 7, pp. 708-716.
ISSN: 0002-8614 CODEN: JAGSAF

COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 020 Gerontology and Geriatrics
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 16 Dec 1991

Last Updated on STN: 16 Dec 1991

AB A variety of neuropharmacologic agents, including anticholinergic drugs, amantadine hydrochloride, levodopa, selegiline, bromocriptine, and pergolide, are now available for the treatment of Parkinson's disease. Of patients treated with dopaminergic agents, 30% develop visual hallucinations, 10% exhibit delusions, 10% have euphoria, 1% have mania, 10% to 15% experience increased anxiety, 15% have confusional periods, and a few exhibit altered sexual behavior. Anticholinergic drugs have a greater tendency to produce confusional states than dopaminergic compounds. Elderly patients and those with underlying dementia are most likely to have untoward side effects with anti-parkinsonism treatment. Dosage reduction is the optimum management strategy, although anti-psychotic agents may be necessary in patients with delusions, and lithium may help control drug-induced mania. Dopaminergic agents share the property of stimulation of D2 dopamine receptors, and this action may play an essential role in mediating their neuropsychiatric effects.

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ACCESSION NUMBER: 1991241637 EMBASE

TITLE: Treating the progressive stages of Parkinson's disease.

AUTHOR: Varon, J., Dr. (correspondence); Jacobs, M.B.

CORPORATE SOURCE: Pulmonary/Crit. Care Med. Div., Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, United States.

SOURCE: Postgraduate Medicine, (1991) Vol. 90, No. 1, pp. 63-64+66+69-71.

ISSN: 0032-5481 CODEN: POMDAS

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 037 Drug Literature Index

008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 16 Dec 1991

Last Updated on STN: 16 Dec 1991

AB Parkinson's disease affects thousands of Americans, men and women equally and apparently with little regard to race. Its diagnosis depends largely on repeated clinical observations of representative signs, such as resting tremor, rigidity, bradykinesia, and gait disturbances. Patients progress through stages: Early disease involves only one limb or side and confers minimal disability, but advanced disease restricts patients to full care. Treatment is chosen on the basis of disease stage and patient response. Combination carbidopa-levodopa (Sinemet) is appropriate for any significant degree of disability, and other antiparkinsonian drugs and anticholinergic agents may be used as adjuncts. Electroconvulsive therapy, use of selegiline hydrochloride (Eldepryl), and surgery are still undergoing investigation but may hold promise.

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ACCESSION NUMBER: 1990048730 EMBASE
TITLE: New concepts in the treatment of Parkinson's disease.
AUTHOR: Ahlskog, J.E.; Wilkinson, J.M.
CORPORATE SOURCE: Mayo Medical School, Rochester, MN, United States.
SOURCE: American Family Physician, (1990) Vol. 41, No. 2,
pp. 574-584.
ISSN: 0002-838X CODEN: AFPYAE
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 1991
Last Updated on STN: 13 Dec 1991

AB Carbidopa/levodopa remains the most potent drug for the treatment of Parkinson's disease. Several newer medications may help stabilize and improve such problems as fluctuating responses to the medication, drug-induced dyskinesias and refractory symptoms. Patients with fluctuating responses that do not respond to adjustments in the carbidopa/levodopa dose may benefit from the addition of a direct-acting dopamine agonist, such as pergolide or bromocriptine. While carbidopa/levodopa and the direct-acting dopamine agonists have a proven track record as symptomatic treatment, they probably do not alter the pathologic process underlying this progressive condition. On the other hand, two studies have shown that selegiline might slow the progression of Parkinson's disease, independent of any direct effects on symptoms.

L17 ANSWER 58 OF 76 Elsevier Biobase COPYRIGHT 2009 Elsevier Science B.V. on STN

ACCESSION NUMBER: 1998132047 ESBIODBASE
TITLE: Transcranial AC pulsed applications of weak electromagnetic fields reduces freezing and falling in progressive supranuclear palsy: A case report
AUTHOR(S): Sandyk, Reuven
CORPORATE SOURCE: Sandyk, Reuven (Department of Neuroscience, Inst. Biomed. Eng. and Rehab. Serv., Touro College, Dix Hills, NY 11746 (US))
SOURCE: International Journal of Neuroscience (May 1998) Volume 94, Number 1-2, pp. 41-54, 91 refs.
CODEN: IJNUB7 ISSN: 0020-7454
COUNTRY OF PUBLICATION: United Kingdom
DOCUMENT TYPE: Journal; Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jan 2009
Last updated on STN: 31 Jan 2009

AN 1998132047 ESBIODBASE

AB Freezing is a common and disabling symptom in patients with Parkinsonism. It affects most commonly the gait in the form of start hesitation and sudden immobility often resulting in falling. A high incidence of freezing occurs in patients with progressive supranuclear palsy (PSP) which is characterized clinically by a constellation of symptoms including supranuclear ophthalmoplegia, postural instability, axial rigidity, dysarthria, Parkinsonism, and pseudobulbar palsy. Pharmacologic therapy of PSP is currently disappointing and the disease progresses relentlessly to a fatal outcome within the first decade after onset. This report concerns a 67 year old woman with a diagnosis of PSP in whom freezing and frequent falling were the most disabling symptoms of the disease at the time of presentation.

Both symptoms, which were rated 4 on the Unified Parkinson Rating Scale (UPRS) which grades Parkinsonian symptoms and signs from 0 to 4, with 0 being normal and 4 being severe symptoms, were resistant to treatment with dopaminergic drugs such as levodopa, amantadine, selegiline and pergolide mesylate as well as with the potent and highly selective noradrenergic reuptake inhibitor nortriptyline. Weekly transcranial applications of AC pulsed electromagnetic fields (EMFs) of picotesla flux density was associated with approximately 50% reduction in the frequency of freezing and about 80-90% reduction in the frequency of falling after a 6 months follow-up period. At this point freezing was rated 2 while falling received a score of 1 on the UPRS. In addition, this treatment was associated with an improvement in Parkinsonian and pseudobulbar symptoms with the difference between the pre- and post EMF treatment across 13 measures being highly significant ($p < .005$; Sign test). These results suggest that transcranial administration AC pulsed EMFs in the picotesla flux density is efficacious in the treatment of PSP.

L17 ANSWER 59 OF 76 Elsevier Biobase COPYRIGHT 2009 Elsevier Science B.V. on STN

ACCESSION NUMBER: 1998069290 ESBIOWBASE
 TITLE: Speech impairment in Parkinson's disease is improved by transcranial application of electromagnetic fields
 AUTHOR(S): Sandyk, Reuven
 CORPORATE SOURCE: Sandyk, Reuven (Department of Neuroscience, Institute for Biomedical Engineering, Rehab. Services of Touro College, Dix Hills, NY 11746 (US))
 SOURCE: International Journal of Neuroscience (Nov 1997) Volume 92, Number 1-2, pp. 63-72, 59 refs.
 CODEN: IJNUB7 ISSN: 0020-7454
 COUNTRY OF PUBLICATION: United Kingdom
 DOCUMENT TYPE: Journal; Article
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 31 Jan 2009
 Last updated on STN: 31 Jan 2009

AN 1998069290 ESBIOWBASE

AB A 52 year old fully medicated physician with juvenile onset Parkinsonism experienced 4 years ago severe 'on-off' fluctuations in motor disability and debilitating speech impairment with severe stuttering which occurred predominantly during 'on-off' periods. His speech impairment improved 20%-30% when sertraline (75 mg/day), a serotonin reuptake inhibitor, was added to his dopaminergic medications which included levodopa, amantadine, selegiline and pergolide mesylate. A more dramatic and consistent improvement in his speech occurred over the past 4 years during which time the patient received, on a fairly regular basis, weekly transcranial treatments with AC pulsed electromagnetic fields (EMFs) of picotesla flux density. Recurrence of speech impairment was observed on several occasions when regular treatments with EMFs were temporarily discontinued. These findings demonstrate that AC pulsed applications of picotesla flux density EMFs may offer a nonpharmacologic approach to the management of speech disturbances in Parkinsonism. Furthermore, this case implicates cerebral serotonergic deficiency in the pathogenesis of Parkinsonian speech impairment which affects more than 50% of patients. It is believed that pulsed applications of EMFs improved this patient's speech impairment through the facilitation of serotonergic transmission which may have occurred in part through a synergistic interaction with sertraline.

L17 ANSWER 60 OF 76 MEDLINE on STN
 ACCESSION NUMBER: 2000512161 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11068454
TITLE: Wearing-off phenomenon--neurological approach.
AUTHOR: Ishikawa A
CORPORATE SOURCE: Department of Neurology, Nishi-Ojiya National Hospital.
SOURCE: Nippon rinsho. Japanese journal of clinical medicine,
(2000 Oct) Vol. 58, No. 10, pp. 2100-3. Ref: 9
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 1 Feb 2001

AB The mechanism of the wearing-off phenomenon and the method of how to control it by means of anti-parkinsonian medications is described. To control the wearing-off phenomenon, it is useful to administer L-dopa before eating because absorption of L-dopa is less when competing with amino acids. Administration of L-dopa four or five times a day is also useful. Dopamin agonists(e.g., bromocriptine, pergolide, talipexole, and cabergoline), and monoamine oxidase inhibitors(e.g., selegiline) control the wearing-off phenomenon, and may also suppress its occurrence. As a specific method for controlling the wearing-off phenomenon, continuous administration of anti-parkinsonian drugs by the intra-alimentary tract or a subcutaneous injection is useful. It is important to avoid early wearing-off phenomenon when treating patients with Parkinson's disease.

L17 ANSWER 61 OF 76 MEDLINE on STN
ACCESSION NUMBER: 2000512155 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11068448
TITLE: The new Parkinson's disease drugs.
AUTHOR: Hasegawa K
CORPORATE SOURCE: Division of Neurology, Sagamihara National Hospital.
SOURCE: Nippon rinsho. Japanese journal of clinical medicine,
(2000 Oct) Vol. 58, No. 10, pp. 2066-71. Ref: 13
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 1 Feb 2001

AB The purpose of the new drugs for Parkinson's disease is control of the long-term levodopa treatment syndromes, especially wearing-off phenomenon and dyskinesia. Therefore, they show long T1/2. Most of them are classified into dopamine agonists. Others are monoamine oxidase B inhibitor and cathecol-o-methyltransferase inhibitor. Marketed dopamine agonists are bromocriptine, pergolide, talipexole, and cabergoline in Japan. Except talipexole, they are all ergot alkaloid derivatives. Their affinity for dopamine receptor is D2 group, and their T1/2 are longer than levodopa. Bromocriptine is an oldest dopamine agonist. Other 3 drugs and bromocriptine had made each other double blinded cross over trial previously. The result of double blinded studies show that their efficacy for PD treatment were equal, 40-50% patients with

PD. However, in clinical usage, some difference is observed as described below. Efficacy of pergolide is strong compared with bromocriptine; however, pergolide is easy to arise dyskinesia. Talipexole is strong in the hypnosis effect. As for cabergoline, it takes long time to show medical effect, so that it is expected to control wearing-off phenomenon. Monoamine oxidase B inhibitor, Selegiline, is useful as an economizer effect to levodopa. As for the cathechole-o-methyltransferase inhibitor (COMT-I) will be make double-blinded trial in future. The efficacy for PD treatment of COMT-I is prolonged levodopa effect for PD, so that wearing-off phenomenon will be controlled. To use these drugs successfully is important with the treatment of PD. In the future, the development of the cause therapy in addition to the systematic therapy is wanted.

L17 ANSWER 62 OF 76 MEDLINE on STN

ACCESSION NUMBER: 1996019379 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 7487655
 TITLE: Treatment of Parkinson's disease.
 AUTHOR: Eadie M J
 CORPORATE SOURCE: Department of Medicine, University of Queensland.
 SOURCE: Australian family physician, (1995 Sep) Vol. 24,
 No. 9, pp. 1685-7, 1690-2.
 Journal code: 0326701. ISSN: 0300-8495.
 PUB. COUNTRY: Australia
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199512
 ENTRY DATE: Entered STN: 24 Jan 1996
 Last Updated on STN: 24 Jan 1996
 Entered Medline: 13 Dec 1995

AB Early stage Parkinson's disease may be better left untreated if it does not limit motor function. Once limitation of function is present levodopa-dopa decarboxylase inhibitor combinations are the most effective therapy, although amantadine may be satisfactory for a time in milder cases. The optimal independent roles of the ergot derivatives bromocriptine and pergolide, and the MAOb inhibitor selegiline, are not yet generally agreed although they are accepted as useful in supplementing the effects of levodopa. With prolonged levodopa use various late-stage treatment problems may appear. The pathogenesis of these is poorly understood and no completely satisfactory ways of managing them are available.

L17 ANSWER 63 OF 76 MEDLINE on STN

ACCESSION NUMBER: 1995266329 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 7747490
 TITLE: Activation by selegiline (Eldepryle) of REM sleep behavior disorder in parkinsonism.
 AUTHOR: Louden M B; Morehead M A; Schmidt H S
 CORPORATE SOURCE: West Virginia University School of Medicine, Morgantown, USA.
 SOURCE: The West Virginia medical journal, (1995 Mar-Apr)
 Vol. 91, No. 3, pp. 101.
 Journal code: 0413777. ISSN: 0043-3284.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: (CASE REPORTS)
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199506
 ENTRY DATE: Entered STN: 21 Jun 1995
 Last Updated on STN: 21 Jun 1995

Entered Medline: 9 Jun 1995

AB Abnormal sleep-wake organization is frequently seen in idiopathic parkinsonism (PD) and other parkinsonism syndromes. A 1993 article in The Annals of Neurology first described the high rate of REM behavior disorder (RBD) in non-demented PD patients (1). In this article, we present the case reports of three non-demented PD patients who manifested RBD while on recommended doses of selegiline (Eldepryle). None of them had problems severe enough to suggest RBD while they were being treated with varying doses of other dopaminergic agents (carbidopa/L-dopa, pergolide) unaccompanied by selegiline.

L17 ANSWER 64 OF 76 MEDLINE on STN
ACCESSION NUMBER: 1994323057 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7914010
TITLE: Initiating treatment for idiopathic parkinsonism.
AUTHOR: Calne D B
CORPORATE SOURCE: Department of Medicine, University of British Columbia, Vancouver, Canada.
SOURCE: Neurology, (1994 Jul) Vol. 44, No. 7 Suppl 6, pp. S19-22. Ref: 10
Journal code: 0401060. ISSN: 0028-3878.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 9 Sep 1994
Last Updated on STN: 6 Feb 1995
Entered Medline: 26 Aug 1994

AB The initial decision in the management of idiopathic parkinsonism is whether any pharmacotherapy is indicated. There is no conclusive evidence that treatment is helpful before symptoms start to affect the patient's life, although some neurologists believe that deprenyl, also known as selegiline, could be useful. Once functional deficits begin to interfere with the patient's work or social activities, treating symptoms becomes appropriate. Anticholinergics and amantadine can be used, but their limited benefit is often accompanied by unacceptable adverse effects. Dopaminomimetics are the most satisfactory medications, including levodopa and such artificial dopamine agonists as bromocriptine, pergolide, or lisuride.

L17 ANSWER 65 OF 76 MEDLINE on STN
ACCESSION NUMBER: 1994203934 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8153048
TITLE: Treatment of Parkinson's disease. From theory to practice.
AUTHOR: Ahlskog J E
CORPORATE SOURCE: Department of Neurology, Mayo Clinic, Rochester, MN 55905.
SOURCE: Postgraduate medicine, (1994 Apr) Vol. 95, No. 5, pp. 52-4, 57-8, 61-4 passim. Ref: 25
Journal code: 0401147. ISSN: 0032-5481.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 23 May 1994
Last Updated on STN: 23 May 1994
Entered Medline: 10 May 1994

AB Parkinson's disease responds rather dramatically to levodopa therapy during the first several years of treatment. With advancing disease, however, symptom control becomes more erratic, and some symptoms may become refractory to treatment. The use of selegiline hydrochloride (Eldepryl) has been proposed to slow the progression of Parkinson's disease; however, current evidence suggests that it is only partially effective at best, and there is no definite proof of a neuroprotective effect. Nonetheless, it is a reasonable treatment choice. Carbidopa-levodopa (Sinemet) remains the foundation of symptomatic treatment of Parkinson's disease. Clinical fluctuations occurring with advancing disease may be at least partially controlled by appropriate adjustments in dosage. A direct-acting dopamine agonist, bromocriptine mesylate (Parlodel) or pergolide mesylate (Permax), can be very helpful as adjunctive therapy to smooth these clinical fluctuations. Excessive intracellular oxidative stress has been proposed as a cause of Parkinson's disease; however, a recent multicenter trial investigating the use of high doses of the antioxidant vitamin E showed it to be ineffective. Whether other forms of nonspecific antioxidant therapy will prove beneficial is open to speculation.

L17 ANSWER 66 OF 76 MEDLINE on STN
ACCESSION NUMBER: 1992261536 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1350053
TITLE: An integrated approach to patient management in Parkinson's disease.
AUTHOR: Lieberman A
CORPORATE SOURCE: Movement Disorders Department, Barrow Neurological Institute, St. Josephs Medical Center, Phoenix, Arizona.
SOURCE: Neurologic clinics, (1992 May) Vol. 10, No. 2, pp. 553-65. Ref: 35
 Journal code: 8219232. ISSN: 0733-8619.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 26 Jun 1992
 Last Updated on STN: 6 Feb 1995
 Entered Medline: 17 Jun 1992

AB New concepts about the pathogenesis and pathophysiology of Parkinson's disease have emerged. For these concepts to be useful, they must be understood, and for them to be applied, the psychology of the patient and the patient's family must be understood. The initial consultation is crucial in establishing a successful relationship between a patient, family, and physician. This consultation is analyzed and ways of avoiding errors and misconceptions delineated. Emphasis is placed on imaginative questioning using the format of the ADL portion of the UPDRS in establishing the diagnosis and following treatment. The rationale for starting treatment with selegiline at this time is discussed in the context of the role that increased MAO-B activity plays in the progression of Parkinson's disease. After making the diagnosis and starting treatment with selegiline, deciding when to start levodopa is the next crucial decision. Often as important as deciding when to start levodopa is overcoming the resistance of the patient to accept this treatment. The next crucial decision occurs after the patient develops response fluctuations on levodopa. A format for assessing the fluctuations is presented, and the merits of different treatments, including selegiline, dopamine agonists (bromocriptine and pergolide), and sustained-release or controlled-release levodopa preparations (Sinemet CR), discussed. The management of patients with depression, sleep problems, and advanced

disease including postural instability and mental changes are reviewed.

L17 ANSWER 67 OF 76 MEDLINE on STN
ACCESSION NUMBER: 1992195439 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1347909
TITLE: Initiating treatment of Parkinson's disease.
AUTHOR: Koller W C
CORPORATE SOURCE: Department of Neurology, University of Kansas Medical Center, Kansas City, KS 66103.
SOURCE: Neurology, (1992 Jan) Vol. 42, No. 1 Suppl 1, pp. 33-8; discussion 57-60. Ref: 67
Journal code: 0401060. ISSN: 0028-3878.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 9 May 1992
Last Updated on STN: 6 Feb 1995
Entered Medline: 20 Apr 1992

AB Treatment of Parkinson's disease (PD) can be divided into two categories: symptomatic therapy (restoring dopamine levels toward normal and reversing functional disability) and preventive therapy (interfering with the pathophysiologic mechanism of PD to prevent or decrease the rate of progression of the disease). Regarding symptomatic treatment, although anticholinergic preparations generally are considered effective for the symptoms of tremor and rigidity without altering bradykinesia, their effectiveness is limited and adverse reactions are common; their role should be restricted to use as adjuvants to levodopa therapy. Amantadine has been shown to be as effective as anticholinergics, but it lacks long-term efficacy. Dopamine agonists--bromocriptine, pergolide mesylate and lisuride in Europe--are not as effective as levodopa and therefore rarely are used as initial therapy; their proposed role, too, is as adjuvants to levodopa therapy. Levodopa is the most effective drug presently available for the treatment of PD; its introduction is accompanied by rapid and dramatic reduction of symptoms and signs. Initial adverse reactions are not usually a major problem; and although there is speculation that initiation of therapy should be delayed because of possible long-term complications, clinically distinguishing these from problems related to disease progression itself is difficult. The possibility that nigral cell death is mediated by oxidative mechanisms provides the basis for considering antioxidant therapy as protective treatment; selegiline, an antioxidant, has been found to delay the need for symptomatic therapy. It is suggested that initial treatment of Parkinson's disease begin with both preventive therapy with selegiline and symptomatic treatment with the sustained-release preparation of levodopa, which may be associated with fewer long-term complications.

L17 ANSWER 68 OF 76 MEDLINE on STN
ACCESSION NUMBER: 1991288348 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1905807
TITLE: Treating the progressive stages of Parkinson's disease.
AUTHOR: Varon J; Jacobs M B
CORPORATE SOURCE: Department of Medicine, Stanford University School of Medicine, California.
SOURCE: Postgraduate medicine, (1991 Jul) Vol. 90, No. 1, pp. 63-6, 69-71.
Journal code: 0401147. ISSN: 0032-5481.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 25 Aug 1991
Last Updated on STN: 25 Aug 1991
Entered Medline: 8 Aug 1991

AB Parkinson's disease affects thousands of Americans, men and women equally and apparently with little regard to race. Its diagnosis depends largely on repeated clinical observations of representative signs, such as resting tremor, rigidity, bradykinesia, and gait disturbances. Patients progress through stages: Early disease involves only one limb or side and confers minimal disability, but advanced disease restricts patients to full care. Treatment is chosen on the basis of disease stage and patient response. Combination carbidopa-levodopa (Sinemet) is appropriate for any significant degree of disability, and other antiparkinsonian drugs and anticholinergic agents may be used as adjuncts. Electroconvulsive therapy, use of selegiline hydrochloride (Eldepryl), and surgery are still undergoing investigation but may hold promise.

L17 ANSWER 69 OF 76 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 1995:274401 SCISEARCH
THE GENUINE ARTICLE: QT862
TITLE: THE RATIONALE FOR THE USE OF DOPAMINE AGONISTS IN PARKINSONS-DISEASE
AUTHOR: JENNER P (Reprint)
CORPORATE SOURCE: UNIV LONDON KINGS COLL, NEURODEGENERAT DIS RES CTR, DIV BIOMED SCI, PHARMACOL GRP, MANRESA RD, LONDON SW3 6LX, ENGLAND (Reprint)
COUNTRY OF AUTHOR: ENGLAND
SOURCE: NEUROLOGY, (MAR 1995) Vol. 45, No. 3, Supp. [3], pp. 6-12.
ISSN: 0028-3878.
PUBLISHER: LITTLE BROWN CO, 34 BEACON STREET, BOSTON, MA 02108-1493.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 51
ENTRY DATE: Entered STN: 1995
Last Updated on STN: 1995

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Experimental and clinical studies indicate that both dopamine D-2-like and D-1-like receptors are important in reversing the motor symptoms of Parkinson's disease, and therefore stimulation of both D-1 and D-2 receptors may be advantageous in its treatment. At present, the role of other receptor subtypes, such as the D-3 receptor, remains unknown, although in primates the D-3 receptor might be of importance because it exists in significant amounts within the caudate-putamen. Both D-1 and D-2 agonists induce dyskinesias in drug-naive, MPTP-treated primates and provoke dyskinesias in levodopa-primed animals. D-1 agonists in low doses, however, might have antiparkinsonian effects without inducing dyskinesias, and on repeated administration perhaps can diminish the intensity of dyskinesias in levodopa-primed, MPTP-treated primates. The production of dyskinesias in Parkinson's disease might reflect an imbalance in the D-1-direct and D-2-indirect GABAergic output pathways from the caudate-putamen, which colocalize tachykinins and enkephalins, respectively. Destruction of the nigrostriatal pathway decreases the mRNA for substance P but elevates the mRNA for enkephalin. Treatment with levodopa reverses the decrease in substance P mRNA but has either a partial or no effect on mRNA for enkephalin. This suggests that levodopa

treatment leads to a new imbalance between output from the striatum through the direct and indirect pathways. In contrast, dopamine agonists appear less able than levodopa to manipulate basal ganglia outflow. This might reflect their decreased ability to reverse parkinsonian motor deficits or the greater ability of levodopa to provoke dyskinesias. Dopamine agonist drugs also might exert neuroprotective actions. Pergolide, like selegiline, elevates superoxide dismutase activity in brain, decreases hydrogen peroxide formation from dopamine, and preserves nigral cells in aging rats. Bromocriptine, apomorphine, and other agonists also scavenge free radicals and show antioxidant activity, compared with the mainly pro-oxidant actions of levodopa.

L17 ANSWER 70 OF 76 TOXCENTER COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 1997:836 TOXCENTER
 COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
 DOCUMENT NUMBER: 34-11266
 TITLE: Drug treatment of Parkinson's disease in the 1990s: achievements and future possibilities
 AUTHOR(S): Hughes, A. J.
 CORPORATE SOURCE: Neurol. Dept., Austin and Repatriation Med. Ctr., Repatriation Campus, Banksia St., West Heidelberg, VIC 3081, Australia
 SOURCE: Drugs (New Zealand), (Feb 1997) Vol. 53, pp. 195-205. 65 Refs.
 CODEN: DRUGAY. ISSN: 0012-6667.
 DOCUMENT TYPE: Journal
 FILE SEGMENT: IPA
 OTHER SOURCE: IPA 97:3096
 LANGUAGE: English
 ENTRY DATE: Entered STN: 16 Nov 2001
 Last Updated on STN: 16 Nov 2001
 AB Advances in the medical treatment of Parkinson disease, current therapies with levodopa, bromocriptine, pergolide, selegiline, amantadine, and anticholinergic agents, and the management of drug induced dyskinesias are discussed.
 Rosemary Gregor

L17 ANSWER 71 OF 76 TOXCENTER COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 1993:51662 TOXCENTER
 DOCUMENT NUMBER: PubMed ID: 8101417
 TITLE: Strategies in the treatment of early Parkinson's disease
 AUTHOR(S): Rinne U K
 CORPORATE SOURCE: Department of Neurology, University of Turku Finland
 SOURCE: Acta neurologica Scandinavica. Supplementum, (1993) Vol. 146, pp. 50-3. Ref: 26.
 Journal code: 0370337. ISSN: 0065-1427.
 COUNTRY: Denmark
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 FILE SEGMENT: MEDLINE
 OTHER SOURCE: MEDLINE 1993325359
 LANGUAGE: English
 ENTRY DATE: Entered STN: 16 Nov 2001
 Last Updated on STN: 31 Jul 2007
 AB Over recent years I have been studying whether dopamine agonist treatment alone, or in early combination with levodopa, might institute a better long-term treatment in Parkinson's disease than levodopa alone. Indeed, early combination of levodopa with bromocriptine, pergolide or lisuride has indicated that this kind of treatment results in better management of Parkinson's disease with fewer fluctuations in disability, especially end-of-dose disturbances and

dyskinesias, than treatment with levodopa alone. Furthermore, similar results were obtained by using lisuride in combination with selegiline and levodopa. Thus, it appears advisable to initiate the dopaminergic treatment in early Parkinson's disease by using a combination of selegiline, levodopa and a dopamine agonist. There are many ways of building up this kind of treatment. Instead of levodopa, it is possible to use initially a dopamine agonist and to add selegiline and levodopa when the therapeutic response becomes insufficient. Another alternative would be to start with selegiline alone, then to add a dopamine agonist and, finally, levodopa when clinically indicated.

L17 ANSWER 72 OF 76 TOXCENTER COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1992:83 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 29-04761
TITLE: Parkinson's disease: update on pharmacologic options to slow progression and treat symptoms
AUTHOR(S): Ahlskog, J. E.
CORPORATE SOURCE: Mayo Clin., Dept. of Neurol., 200 First St. SW, Rochester, MN 55905, USA
SOURCE: Hospital Formulary (USA), (Feb 1992) Vol. 27, pp. 146-152, 161-163. 92 Refs. CODEN: HOFOD9. ISSN: 0098-6909.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 92:231
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB Parkinson's disease, including therapy for early and late disease, results of clinical studies, drug interactions, adverse effects, and costs of medications, is discussed. Drug therapy with such agents as selegiline, alpha-tocopherol, levodopa, bromocriptine, pergolide, carbidopa/levodopa (Sinemet CR), and adjunctive therapy with baclofen (Lioresal) and antidepressants are included.
Kate Gibbons

L17 ANSWER 73 OF 76 TOXCENTER COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:2681 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 29-08653
TITLE: Drug therapy for Parkinson's disease
AUTHOR(S): Shimp, L. A.
SOURCE: Journal Michigan Pharmacist, (Dec 1991) Vol. 29, pp. 448-451, 453. ISSN: 0026-2404.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 91:11025
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB The pathologic brain changes that cause the signs and symptoms of Parkinson's disease and the use and side effects of anticholinergics, levodopa-carbidopa, amantadine, bromocriptine, pergolide, and selegiline are discussed. This article qualifies for one hour of U.S. CE credit by the ACPE.
Anne L. Morisseau

L17 ANSWER 74 OF 76 TOXCENTER COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1990:481 TOXCENTER

COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 27-12453
TITLE: New alternatives for the treatment of Parkinson's disease
AUTHOR(S): Erwin, W. G.
CORPORATE SOURCE: Philadelphia Coll. of Pharm. and Sci., Philadelphia, PA, USA
SOURCE: American Druggist (USA), (Feb 1990) Vol. 201, pp. 62, 64, 66, 68, 70, 72.
CODEN: AMDRAG. ISSN: 0190-5279.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 90:1519
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB The pathophysiology, clinical symptoms and treatment of Parkinson disease are discussed. Long term complications of levodopa therapy and the use, dosage and problems associated with pergolide mesylate (Permax) and selegiline hydrochloride (Eldepryl) are described. This article qualifies for 2 hours U.S. CE credit by the ACPE.
Ellen Katz Neumann

L17 ANSWER 75 OF 76 TOXCENTER COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1989:1668 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 27-03204
TITLE: Pergolide and selegiline for Parkinson's disease
AUTHOR(S): anon
SOURCE: Medical Letter on Drugs and Therapeutics (USA), (Sep 8 1989) Vol. 31, pp. 81-83. 16 Refs.
CODEN: MELEAP. ISSN: 0025-732X.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 89:5438
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB The pharmacology, pharmacokinetics, clinical effectiveness, adverse effects and dosage of 2 newly approved antiparkinson agents, pergolide mesylate (Permax) and selegiline hydrochloride (Eldepryl) are reported.
Victor Origoni

L17 ANSWER 76 OF 76 TOXCENTER COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1988:2925 TOXCENTER
COPYRIGHT: Copyright (c) 2009 The Thomson Corporation
DOCUMENT NUMBER: 26-11477
TITLE: Drugs for parkinsonism
AUTHOR(S): anon
SOURCE: Medical Letter on Drugs and Therapeutics (USA), (Dec 16 1988) Vol. 30, pp. 113-116.
CODEN: MELEAP. ISSN: 0025-732X.
DOCUMENT TYPE: Journal
FILE SEGMENT: IPA
OTHER SOURCE: IPA 88:10326
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2001
Last Updated on STN: 16 Nov 2001

AB The mechanism of action, clinical effects, limitations, and adverse effects of drugs used in the treatment of Parkinson disease are presented. Drugs covered include levodopa alone and in combination with carbidopa (Sinemet), bromocriptine mesylate (Parlodel), anticholinergic

agents, amantadine hydrochloride (Symmetrel), selegiline hydrochloride (Eldepryl), pergolide (Permax), lisuride, controlled release Sinemet, and adjunctive antidepressants.
Lisa Webster

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